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(54) Title: CRYSTALLOGRAPHIC STRUCTURE OF THE ANDROGEN RECEPTOR LIGAND BINDING DOMAIN

(57) Abstract: The first crystal structure of the androgen receptor ligand binding domain has been determined to 2.0 angstrom resolution. Disclosed are the coordinates for the crystal structure, and methods for determining agonists, partial agonists, antagonists, partial antagonists, and selective androgen receptors modulators (SARMS) of the androgen receptor.

CRYSTALLOGRAPHIC STRUCTURE OF THE ANDROGEN RECEPTOR LIGAND BINDING DOMAIN

Field of Invention

The present invention relates to compositions and crystals of androgen receptor ligand binding domain optionally in complex with its ligand. This invention also relates to methods of using the structure coordinates of the androgen receptor ligand binding domain /ligand complex to solve the structure of similar or homologous proteins or protein complexes. This invention also relates to methods for designing and selecting ligands that bind to the androgen receptor and methods of using such ligands.

Background of the Invention

The androgen receptor (AR) is a member of the steroid nuclear-receptor superfamily of ligand-dependent transcription factors. The binding of androgen to AR initiates the gene activation required for male sex development.

AR is an important target primarily in two drug discovery areas. In oncology drug discovery, inhibitors (antagonists or partial antagonists) of androgen receptor function are useful for treatment of anti-androgen refractory prostate cancer. In metabolic diseases drug discovery, agonists or partial agonists to the androgen receptor in muscle are useful to treat age-related diseases.

As with the other members of the steroid receptor family, AR has several functional domains including a DNA binding domain (DBD), and a 261 residue ligand-binding domain (LBD) (Mw = 30,245 Da) which contains the androgen binding site, and is responsible for switching on the androgen function.

Development of synthetic ligands that specifically bind to androgen receptors has been largely guided by trial and error method of drug design despite the importance of the androgen receptor in physiological processes and medical conditions such as prostate cancer and modulation of reproductive organ modulation. Previously, new ligands specific for androgen receptors were discovered in the absence of information on the three dimensional structure of the androgen receptor with a bound ligand. Before the present invention, researchers were

essentially discovering androgen receptor ligands by probing in the dark and without the ability to visualize how the amino acids of the androgen receptor held a ligand in its grasp.

Consequently, it would be advantageous to devise methods and compositions for reducing the time required to discover ligands to the androgen receptor, synthesize such compounds and administer such compounds to organisms to modulate physiological processes regulated by the androgen receptor.

The cDNA and amino acid sequences of human and rat androgen receptors have been described (Proc. Natl. Acad. Sci. U.S.A. 1988 85: 7211-7215). However, there have been no crystals reported of any androgen receptor. Thus, x-ray crystallographic analysis of such proteins has not been possible.

We have discovered the first crystal structure of the androgen receptor ligand binding domain (AR-LBD). Our understanding or the androgen receptor structure has allowed for the determination of the ligand binding site for selective androgen receptor modulators (SARMs).

Summary of the Invention

The present invention provides crystals of AR-LBD and crystals of an AR-LBD bound to a ligand, i.e. an AR-LBD/AR-LBD ligand complex. Most preferably the AR-LBD ligand is dihydrotestosterone (DHT). Thus, the present invention is directed to a crystal of an AR-LBD comprising:

1) an AR-LBD and an AR-LBD ligand or

2) an AR-LBD without an AR-LBD ligand;

wherein said crystal diffracts to at least 3 angstrom resolution and has a crystal stability within 5% of its unit cell dimensions. The crystal of AR or AR-LBD preferably has at least 200 amino acid and preferably comprises amino acid sequence 672 to 917 of rat AR or the AR amino acid sequence 672 to 917 of human AR.

The present invention also provides the structure coordinates of the AR-LBD/AR-LBD ligand complex. The complete coordinates are listed in Table A.

The present invention also provides a method for determining at least a portion of the three-dimensional structure of molecules or molecular complexes which contain at least some structurally similar

features to the androgen receptor ligand binding domain. It is preferred that these molecules or molecular complexes comprise at least a part of the ligand binding site defined by structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877 and F878 according to Table A, or a mutant or homologue thereof. Since the protein sequences for rat and human AR LBD are identical, the human numbering system was used herein.

The present invention also provides a machine-readable data storage medium which comprises a data storage material encoded with machine readable data defined by the structure coordinates of an AR-LBD/AR-LBD ligand or ligand complex according to Table A or a homologue of the complex.

The present invention further provides a binding site in AR-LBD for an AR-LBD ligand as well as methods for designing or selecting AR modulators including agonists, partial agonists, antagonists, partial antagonists and/or selective androgen receptor modulators (SARMs) of AR using information about the crystal structures disclosed herein.

Brief Description of the Drawing

Figure 1 is a ribbon style drawing of the Androgen Receptor LBD. The substrate DHT is shown as a ball-and-stick figure.

Figure 2 is a comparison of the androgen receptor ligand binding domain with progesterone receptor ligand binding domain.

Figure 3 provides three views of the omit electron density map of dihydrotestosterone (DHT) in the hormone-binding site of AR-LBD. There are hydrogen bonds between the steroid and the side chains of Arg 752 and Asn 705.

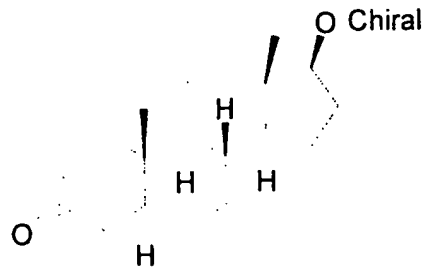
Figure 4 is a comparison of the binding of dihydrotestosterone to AR-LBD (top) and of progesterone to PR-LBD (bottom). Note that an additional hydrogen bond interaction would be possible if both the sidechains of both N719 and the progesterone were flipped.

Detailed Description of the Invention

The first crystal structure of the androgen receptor ligand binding domain (AR-LBD) has been determined to 2.0 Å resolution.

Crystals of rat AR-LBD were grown from precipitating solutions containing 0.9 M Sodium Tartrate, 0.1 M Na Hepes, pH 7.5. X-ray diffraction from the crystals have the symmetry and systematic absences of the orthorhombic space group P212121 with unit cell dimensions a = 56.03 Å , b = 66.27 Å, c= 70.38 Å, and one molecule per asymmetric unit (Mathews Volume = 2.16 $Å^3$ Da^{-1}). The structure was determined by the method of molecular replacement using the structure of the Progesterone Receptor LBD (PR-LBD) as the search model.

The complex of AR-LBD with dihydrotestosterone (DHT) shows the mode of binding of the steroid to the receptor in the agonist conformation.



Dihydrotestosterone

The following abbreviations are used throughout the application:

A = Ala = Alanine
V = Val = Valine
L = Leu = Leucine
I = Ile = Isoleucine
P = Pro = proline
F = Phe = phenylalanine
W = Trp = Tryptophan
M = Met = Methionine
G = Gly = Glycine
S = Ser = Serine
T = Thr = Threonine
C = Cys = Cysteine
Y = Tyr = Tyrosine
N =Asn = Asparagine

Q =Gln = Glutamine
D = Asp = Aspartic Acid
E = Glu = Glutamic Acid
K = Lys = Lysine
R = Arg = Arginine
H = His = Histidine

"Atom type" refers to the element whose coordinates have been determined. Elements are defined by the first letter in the column.

"X, Y, Z" crystallographically define the atomic position determined for each atom.

"B" is a thermal factor that measures movement of the atom around its atomic center.

"Occ" is an occupancy factor that refers to the fraction of the molecules in which each atom occupies the position specified by the coordinates. A value of "1" indicates that each atom has the same conformation, i.e., the same position, in all molecules of the crystal.

Additional definitions are set forth in the specification where necessary.

The androgen receptor (AR) described herein is intended to include any polypeptide which has the activity of the naturally occurring androgen receptor . The AR and AR-LBD contemplated herein includes all vertebrate and mammalian forms such as rat, mouse, pig, goat, horse, guinea pig, rabbit, monkey, orangutan and human. Such terms also include polypeptides that differ from naturally occurring forms of AR and AR-LBD by having amino acid deletions, substitutions, and additions, but which retain the activity of AR and AR-LBD, respectively. The crystal structure of the invention preferably contains at least 25%, more preferably at least 50%, more preferably at least 75%, more preferably at least 90%, more preferably at least 95%, more preferably at least 99%, and most preferably all of the coordinates listed in Table A. The crystal of the AR-LBD/AR-LBD ligand of the invention preferably has the following unit cell dimensions in angstroms: $a = 56.03 \pm 5\%$, b

= 66.27 ± 5%, c = 70.38 ± 5% and an orthorhombic space group P212121.

The AR-LBD ligand of this invention is any peptide, peptide mimetic or nonpeptide, including small organic molecules, that is capable of acting as a ligand for AR-LBD. In a preferred embodiment, the AR-LBD ligand is an AR modulator. By "AR modulator" it is meant an agonist or activator, a partial agonist or partial activator, an antagonist or inhibitor, or a partial antagonist or partial inhibitor which demonstrates tissue specific activations of the AR. Such compounds are also referred to herein as SARMs (selective androgen receptor modulators) of the AR-LBD. Examples of preferred agonists include androgens such as dihydrotestosterone.

The peptides referred to herein (e.g., AR, AR-LBD, and the like) may be produced by any well-known method, including synthetic methods, such as solid phase, liquid phase and combination solid phase/liquid phase syntheses; recombinant DNA methods, including cDNA cloning, optionally combined with site directed mutagenesis; and/or purification of the natural products, optionally combined with enzymatic cleavage methods to produce fragments of naturally occurring

Advantageously, the crystallizable compositions provided by this invention are amenable to x-ray crystallography. Thus, this invention also provides the three-dimensional structure of the AR-LBD/AR-LBD ligand complex, particularly the complex of rat AR-LBD with dihydrotestosterone.

The three-dimensional structure of the AR-LBD / dihydrotestosterone complex of this invention is defined by a set of structure coordinates as set forth in Table A. The term "structure coordinates" refers to Cartesian coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of an androgen receptor/dihydrotestosterone complex in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are then used to establish the positions of the individual atoms of the complex.

Those of skill in the art will understand that a set of structure coordinates for a receptor or receptor/ligand complex or a portion

thereof, is a relative set of points that define a shape in three dimensions. Thus, it is possible that an entirely different set of coordinates could define a similar or identical shape. Moreover, slight variations in the individual coordinates will have little effect on overall shape.

The variations in coordinates discussed above may be generated because of mathematical manipulations of the structure coordinates. For example, the structure coordinates set forth in Table A could be manipulated by crystallographic permutations of the structure coordinates, fractionalization of the structure coordinates; integer additions or subtractions to sets of the structure coordinates, inversion of the structure coordinates or any combination of the above.

Alternatively, modifications in the crystal structure due to mutations, additions, substitutions, and/or deletions of amino acids, or other changes in any of the components that make up the crystal could also account for variations in structure coordinates. If such variations are within an acceptable standard error as compared to the original coordinates, the resulting three-dimensional shape is considered to be the same.

Various computational analyses are therefore necessary to determine whether a molecule or molecular complex or a portion thereof is sufficiently similar to all or parts of the androgen receptor/dihydrotestosterone described above as to be considered the same. Such analyses may be carried out in current software applications, such as the Molecular Similarity application of QUANTA (Molecular Simulations Inc., San Diego, CA) version 4.1, and as described in the accompanying User's Guide.

The Molecular Similarity application permits comparisons between different structures, different conformations of the same structure, and different parts of the same structure. The procedure used in Molecular Similarity to compare structures is divided into four steps: 1) load the structures to be compared; 2) define the atom equivalences in these structures; 3) perform a fitting operation; and 4) analyze the results.

Each structure is identified by a name. One structure is identified as the target (i.e., the fixed structure); all remaining structures

are working structures (i.e., moving structures). Since atom equivalency within QUANTA is defined by user input, for the purpose of this invention we will define equivalent atoms as protein backbone atoms (N, Cs, C and O) for all conserved residues between the two structures being compared. We will also consider only rigid fitting operations.

When a rigid fitting method is used, the working structure is translated and rotated to obtain an optimum fit with the target structure. The fitting operation uses an algorithm that computes the optimum translation and rotation to be applied to the moving structure, such that the root mean square difference of the fit over the specified pairs of equivalent atom is an absolute minimum. This number, given in angstroms, is reported by QUANTA.

For the purpose of this invention, any molecule or molecular complex that has a root mean square deviation of conserved residue backbone atoms (N, Cα, C, O) of less than 1.5 Å when superimposed on the relevant backbone atoms described by structure coordinates listed in Table A are considered identical. More preferably, the root mean square deviation is less than 1.0 Å. In a preferred embodiment of the present invention, the molecule or molecular complex comprises at least a portion of the ligand binding site defined by structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877 and F878 according to Table A, or a mutant or homologue of said molecule or molecular complex. More preferred are molecules or molecular complexes comprising all or any part of the ligand binding site defined by structure coordinates of AR-LBD amino acids N705, Q711, R752, F764 and T877 according to Table A, or a mutant or homologue of said molecule or molecular complex. Since the protein sequences for rat and human AR LBD are identical, the human numbering system has been used herein.

The term "complex" or "molecular complex" means AR-LBD or a mutant or homologue of AR-LBD in a covalent or non-covalent association with a chemical entity or compound.

For purposes of the present invention, by "at least a portion of" it is meant all or any part of the ligand binding site defined by these structure coordinates.

By "mutant or homologue" as used herein it is meant a molecule or molecular complex having a similar structure and/or sequences to AR-LBD. By "similar structure" it is meant a mutant or homologue having a binding pocket that has a root mean square deviation from the backbone atoms of said AR-LBD amino acids of not more than 1.5 Angstroms. By "similar sequence" it is meant a mutant or homologue having 30%, or more preferably 75%, identity with AR-LBD.

The term "root mean square deviation" means the square root of the arithmetic mean of the squares of the deviations from the mean. It is a way to express the deviation or variation from a trend or object. For purposes of this invention, the "root mean square deviation" defines the variation in the backbone of a protein or protein complex from the relevant portion of the backbone of the AR portion of the complex as defined by the structure coordinates described herein.

Once the structure coordinates of a protein crystal have been determined they are useful in solving the structures of other crystals.

Thus, in accordance with the present invention, the structure coordinates of an androgen receptor/dihydrotestosterone complex, and in particular a complex, and portions thereof is stored in a machine-readable storage medium. Such data may be used for a variety of purposes, such as drug discovery and x-ray crystallographic analysis or protein crystal.

Accordingly, in one embodiment of this invention is provided a machine-readable data storage medium comprising a data storage material encoded with the structure coordinates set forth in Table A.

One embodiment utilizes System 10 as disclosed in WO 98/11134, the disclosure of which is incorporated herein by reference in its entirety

For the first time, the present invention permits the use of structure-based or rational drug design techniques to design, select, and synthesize chemical entities, including inhibitory and stimulatory compounds that are capable of binding to AR-LBD, or any portion thereof.

One particularly useful drug design technique enabled by this invention is iterative drug design. Iterative drug design is a method for optimizing associations between a protein and a compound by determining and evaluating the three-dimensional structures of successive sets of protein/compound complexes.

Those of skill in the art will realize that association of natural ligands or substrates with the binding pockets of their corresponding receptors or enzymes is the basis of many biological mechanisms of action. The term "binding pocket" as used herein, refers to a region of a molecule or molecular complex, that, as a result of its shape, favorably associates with another chemical entity or compound. Similarly, many drugs exert their biological effects through association with the binding pockets of receptors and enzymes. Such associations may occur with all or any parts of the binding pockets. An understanding of such associations will help lead to the design of drugs having more favorable associations with their target receptor or enzyme, and thus, improved biological effects. Therefore, this information is valuable in designing potential ligands or inhibitors of receptors or enzymes, such as inhibitors of AR.

The term "associating with" refers to a condition of proximity between chemical entities or compounds, or portions thereof. The association may be non-covalent -- wherein the juxtaposition is energetically favored by hydrogen bonding or van der Waals or electrostatic interactions -- or it may be covalent.

In iterative drug design, crystals of a series of protein/compound complexes are obtained and then the three-dimensional structures of each complex is solved. Such an approach provides insight into the association between the proteins and compounds of each complex. This is accomplished by selecting compounds with inhibitory activity, obtaining crystals of this new protein/compound complex, solving the three dimensional structure of the complex, and comparing the associations between the new protein/compound complex and previously solved protein/compound complexes. By observing how changes in the compound affected the protein/compound associations, these associations may be optimized.

In some cases, iterative drug design is carried out by forming successive protein-compound complexes and then crystallizing each new complex. Alternatively, a pre-formed protein crystal is soaked in the presence of an inhibitor, thereby forming a protein/compound complex and obviating the need to crystallize each individual protein/compound complex.

As used herein, the term "soaked" refers to a process in which the crystal is transferred to a solution containing the compound of interest.

The structure coordinates set forth in Table A can also be used to aid in obtaining structural information about another crystallized molecule or molecular complex. This may be achieved by any of a number of well-known techniques, including molecular replacement.

The structure coordinates set forth in Table A can also be used for determining at least a portion of the three-dimensional structure of molecules or molecular complexes which contain at least some structurally similar features to AR. In particular, structural information about another crystallized molecule or molecular complex may be obtained. This may be achieved by any of a number of well-known techniques, including molecular replacement.

Therefore, in another embodiment this invention provides a method of utilizing molecular replacement to obtain structural information about a crystallized molecule or molecular complex whose structure is unknown comprising the steps of:

a) generating an X-ray diffraction pattern from said crystallized molecule or molecular complex;

b) applying at least a portion of the structure coordinates set forth in Table A to the X-ray diffraction pattern to generate a three-dimensional electron density map of the molecule or molecular complex whose structure is unknown; and

c) using all or a portion of the structure coordinates set forth in Table A to generate homology models of AR-LBD or any other nuclear hormone receptor ligand binding domain.

Preferably, the crystallized molecule or molecular complex is obtained by soaking a crystal of this invention in a solution.

By using molecular replacement, all or part of the structure coordinates of the AR-LBD/AR-LBD ligand complex provided by this invention or molecular complex whose structure is unknown more quickly and efficiently than attempting to determine such information ab initio.

Molecular replacement provides an accurate estimation of the phases for an unknown structure. Phases are a factor in equations used to solve crystal structures that can not be determined directly. Obtaining accurate values for the phases, by methods other than molecular replacement, is a time-consuming process that involves iterative cycles of approximations and refinements and greatly hinders the solution of crystal structures. However, when the crystal structure of a protein containing at least a homologous portion has been solved, the phases from the known structure provide a satisfactory estimate of the phases for the unknown structure.

Thus, this method involves generating a preliminary model of a molecule or molecular complex whose structure coordinates are unknown, by orienting and positioning the relevant portion of the AR-LBD/AR-LBD ligand complex according to Table A within the unit cell of the crystal of the unknown molecule or molecular complex so as best to account for the observed X-ray diffraction pattern of the crystal of the molecule or molecular complex whose structure is unknown. Phases can then be calculated from this model and combined with the observed X-ray diffraction pattern amplitudes to generate an electron density map of the structure whose coordinates are unknown. This, in turn, can be subjected to any well-known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallized molecule or molecular complex [E. Lattman, "Use of the Rotation and Translation Functions", in Meth. Enzymol., 115, pp. 55-77 (1985); M. G. Rossmann, ed., "The Molecular Replacement Method", Int. Sci. Rev. Set., No. 13, Gordon & Breach, New York (1972)].

The structure of any portion of any crystallized molecule or molecular complex, or mutant, homologue or orphan receptor that is sufficiently homologous to any portion of the AR-LBD/AR-LBD ligand complex can be solved by this method. Along with the aforementioned AR, there also exist a number of AR for which the activating or

deactivating ligands may not be characterized. These proteins are classified as AR due to strong sequence homology to other AR, and are known as orphan receptors.

The structure coordinates are also particularly useful to solve the structure of crystals of AR-LBD/AR-LBD ligand co-complexed with a variety of chemical entities. This approach enables the determination of the optimal sites for interaction between chemical entities, including interaction of candidate AR inhibitors with the complex. For example, high resolution X-ray diffraction data collected from crystals exposed to different types of solvent allows the determination of where each type of solvent molecule resides. Small molecules that bind tightly to these sites can then be designed and synthesized and tested for their AR inhibition activity.

All of the complexes referred to above may be studied using well-known X-ray diffraction techniques and may be refined versus 1.5-3 A resolution X-ray data to an R value of about 0.20 or less using computer software, such as X-PLOR [Yale University, 1992, distributed by Molecular Simulations, Inc.; see, e.g., Blundell & Johnson, supra; Meth. Enzymol., vol. 114 & 115, H. W. Wyckoff et al., eds., Academic Press (1985)]. This information may thus be used to optimize known AR agonists, partial agonists, antagonists, partial antagonists and SARMS, and more importantly, to design new AR agonists/antagonists.

Accordingly, the present invention is also directed to a binding site in AR-LBD for an AR-LBD ligand in which a portion of AR-LBD ligand is in van der Walls contact or hydrogen bonding contact with at least one of the following residues: V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD. For purposes of this invention, by AR-LBD binding site it is also meant to include mutants or homologues thereof. In a preferred embodiment, the mutants or homologues have at least 25% identity, more preferably 50% identity, more preferably 75% identity, and most preferably 95% identity to residues V685, L700, L701, S702, S703, L704, N705, E706, L707,

G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD binding sites.

The present invention is also directed to a machine-readable data storage medium, comprising a data storage material encoded with machine readable data, wherein the data is defined by the structure coordinates of an AR-LBD/AR-LBD ligand according to Table A or a homologue of said complex, wherein said homologue comprises backbone atoms that have a root mean square deviation from the backbone atoms of the complex of not more than 3.0Å. Preferably, the machine-readable data storage medium, according to the invention, is wherein said molecule or molecular complex is defined by the set of structure coordinates for AR-LBD/AR-LBD ligand according to Table A, or a homologue of said molecule or molecular complex, said homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 2.0 Å. In a preferred embodiment the machine-readable data storage medium comprises a data storage material encoded with a first set of machine readable data comprising a Fourier transform of at least a portion of the structural coordinates for an AR-LBD/AR-LBD ligand according to Table A; which, when combined with a second set of machine readable data comprising an X-ray diffraction pattern of a molecule or molecular complex of unknown structure, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, said first set of data and said second set of data.

The present invention also provides for computational methods using three dimensional models of the androgen receptor that are based on crystals of AR-LBD/AR-LBD ligand complex. Generally, the computational method of designing an androgen receptor ligand determines which amino acid or amino acids of the AR-LBD interact with a chemical moiety (at least one) of the ligand using a three dimensional model of a crystallized protein comprising the AR-LBD with a bound ligand, and selecting a chemical modification (at least one) of the

chemical moiety to produce a second chemical moiety with a structure that either decreases or increases an interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the corresponding chemical moiety on the natural hormone.

The computational methods of the present invention are for designing androgen receptor synthetic ligands using such crystal and three dimensional structural information to generate synthetic ligands that modulate the conformational changes of the androgen receptor's LBD. These computational methods are particularly useful in designing an agonist, partial agonist, antagonist or partial antagonist or SARMs to the androgen receptor, wherein the agonist, partial agonist, antagonist or partial antagonist or SARMS has an extended moiety that prevents any one of a number of ligand-induced molecular events that alter the receptor's influence on the regulation of gene expression, such as preventing the normal coordination of the activation domain observed for a naturally occurring ligand or other ligands that mimic the naturally occurring ligand, such as an agonist. As described herein, synthetic ligands of the androgen receptor will be useful in modulating androgen receptor activity in a variety of medical conditions.

AR is known to comprise various domains as follows:

1) a variable amino-terminal domain;

2) a highly conserved DNA-binding domain (DBD); and

3) a less conserved carboxyl-terminal ligand-binding domain (LBD).

This modularity permits different domains of each protein to separately accomplish different functions, although the domains can influence each other. The separate function of a domain is usually preserved when a particular domain is isolated from the remainder of the protein. Using conventional protein chemistry techniques a modular domain can sometimes be separated from the parent protein. Using conventional molecular biology techniques each domain can usually be separately expressed with its original function intact or chimerles of two different nuclear receptors can be constructed, wherein the chimetics retain the properties of the individual functional domains of thc respective nuclear receptors from which the chimerica were generated.

Amino Terminal Domain

The amino terminal domain is the least conserved of the three domains. This domain is involved in transcriptional activation and in some cases its uniqueness may dictate selective receptor-DNA binding and activation of target genes by specific receptor isoforms. This domain can display synergistic and antagonistic interactions with the domains of the LBD. For example, studies with mutated and/or deleted receptors show positive cooperativity of the amino and carboxy terminal domains. In some cases, deletion of either of these domains will abolish the receptor's transcriptional activation functions.

DNA-Binding Domain

The DBD is the most conserved domain. The DBD contains two perpendicularly oriented a-helixes that extend from the base of the first and second zinc fingers. The two zinc fingers function in concert along with non-zinc finger residues to direct nuclear receptors to specific target sites on DNA and to align receptor homodimer or heterodimer interfaces. Various amino acids in DBD influence spacing between two half-sites for receptor dimer binding.

Ligand or AR Binding Domain

The LBD is the second most highly conserved domain. Whereas integrity of several different LBD sub-domains is important for ligand binding, truncated molecules containing only the LBD retain normal ligand-binding activity. This domain also participates in other functions, including dimerization, nuclear translocation and transcriptional activation. Importantly, this domain is the binding site for ligands, i.e. AR modulators, and undergoes ligand-induced conformational changes as detailed herein.

As described herein, the LBD of AR can be expressed, crystallized, its three dimensional structure determined with a ligand bound (either using crystal data from the same receptor or a different receptor or a combination thereof), and computational methods used to design ligands to its LBD, particularly ligands that contain an extension moiety that coordinates the activation domain of AR.

Once a computationally designed ligand (CDL) is synthesized, it can be tested using assays to establish its activity as an agonist, partial agonist, antagonist or partial antagonist or SARM, and affinity, as described herein. After such testing, the CDLs can be further refined by

generating LBD crystals with a CDL bound to the LBD. The structure of the CDL can then be further refined using the chemical modification methods described herein for three dimensional models to improve the activity or affinity of the CDL and make second generation CDLs with improved properties, such as that of a super agonist or antagonist.

Typically AR-LBD is purified to homogeneity for crystallization. Purity of AR-LBD is measured with SDS-PAGE, mass spectrometry and hydrophobic HPLC. The purified AR for crystallization should be at least 97.5 % pure or 97.5%, preferably at least 99.0% pure or 99.0% pure, more preferably at least 99.5% pure or 99.5% pure.

Initially purification of the unliganded receptor can be obtained by conventional techniques, such as hydrophobic interaction chromatography (HPLC), ion exchange chromatography (HPLC), and heparin affinity chromatography.

To achieve higher purification for improved crystals of AR, it will be desirable to ligand shift purify the nuclear receptor using a column that separates the receptor according to charge, such as an ion exchange or hydrophobic interaction column, and then bind the eluted receptor with a ligand, especially an agonist or partial agonist. The ligand induces a change in the receptor's surface charge such that when re-chromatographed on the same column, the receptor then elutes at the position of the liganded receptor are removed by the original column run with the unliganded receptor. Usually saturating concentrations of ligand are used in the column and the protein can be preincubated with the ligand prior to passing it over the column.

More recently developed methods involve engineering a "tag" such as with histidine placed on the end of the protein, such as on the amino terminus, and then using a nickle chelation column for purification, Janknecht R., Proc. Natl. Acad.Sci. USA Vol 88:8972-8976 (1991) incorporated by reference.

To determine the three dimensional structure of a AR-LBD, it is desirable to co-crystalize the LBD with a corresponding LBD ligand.

Typically purified AR-LBD is equilibrated at a saturating concentration of ligand at a temperature that preserves the integrity of the protein. Ligand equilibration can be established between 2 and 37° C, although the receptor tends to be more stable in the 2-20° C range.

Preferably crystals are made with the hanging drop methods. Regulated temperature control is desirable to improve crystal stability and quality. Temperatures between 4 and 25°C are generally used and it is often preferable to test crystallization over a range of temperatures. It is preferable to use crystallization temperatures from 18 to 25°C, more preferably 20 to 23°C, and most preferably 22°C.

Ligands that interact with AR can act as an agonist, partial agonist, antagonist or partial antagonist or SARM based on what ligand-induced conformational changes take place.

Agonists or partial agonists induce changes in receptors that place them in an active conformation that allows them to influence transcription, either positively or negatively. There may be several different ligand-induced changes in the receptor's conformation.

Antagonists or partial antagonists bind to receptors, but fail to induce conformational changes that alter the receptor's transcriptional regulatory properties or physiologically telcram conformations. Binding of an antagonist or partial antagonist can also block the binding and therefore the actions of an agonist or partial agonist.

Partial agonists, or partial antagonists, bind to receptors and induce only part of the changes in the receptors that are induced by agonists or antagonists, respectively. The differences can be qualitative or quantitative. Thus, a partial agonist or partial antagonist may induce some of the conformation changes induced by agonists or antagonists, respectively, but not others, or it may only induce certain changes to a limited extent.

As described herein, the unliganded receptor is in a configuration that is either inactive, has some activity or has repressor activity. Binding of agonist ligands induces conformational changes in the receptor such that the receptor becomes more active, either to stimulate or repress the expression of genes. The receptors may also have non-genomic actions, some of the known types of changes and/or the sequelae of these are listed herein.

Heat shock protein binding domains present a region for binding to the LBD and can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that stabilizes the binding or comact of the heat shock protein binding

domain with the LBD can be designed. Typically such chemical moieties will extend past and away from the molecular recognition domain on the ligand and usually past the buried binding cavity of the ligand.

Ligand binding by the receptor is a dynamic process, which regulates receptor function by inducing an altered conformation.

The three-dimensional structure of the liganded AR receptor will greatly aid in the development of new AR synthetic ligands. In addition, AR is overall well suited to modern methods including three-dimensional structure elucidation and combinatorial chemistry such as those disclosed in EP 335 628, U.S. patent 5,463,564, which are incorporated herein by reference. Computer programs that use crystallography data when practicing the present invention will enable the rational design of ligand to AR. Programs such as RASMOL can be used with the atomic coordinates from crystals generated by practicing the invention or used to practice the invention by generating three dimensional models and/or determining the structures involved in ligand binding. Computer programs such as INSIGHT and GRASP allow for further manipulation and the ability to introduce new structures. In addition, high throughput binding and bioactivity assays can be devised using purified recombinant protein and modern reporter gene transcription assays described herein and known in the art in order to refine the activity of a CDL.

Generally the computational method of designing an AR synthetic ligand comprises two steps:

1) determining which amino acid or amino acids of AR- LBD interacts with a first chemical moiety (at least one) of the ligand using a three dimensional model of a crystallized protein comprising an AR-LBD with a bound ligand; and

2) selecting a chemical modifications (at least one) of the first chemical moiety to produce a second chemical moiety with a structure to either decrease or increase an interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the first chemical moiety.

Preferably the method is carried out wherein said three dimensional model is generated by comparing isomorphous ligand derivatives to produce improved phasing. Further preferred is wherein said method

comprises determining a change in interaction between said interacting amino acid and said ligand after chemical modification of said first chemical moiety, especially wherein said three dimensional model is generated by comparing isomorphous ligand derivatives to produce improved phasing. Also preferred is wherein said selecting uses said first chemical moiety that interacts with at least one of the interacting amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906.

As shown herein, interacting amino acids form contacts with the ligand and the center of the atoms of the interacting amino acids are usually 2 to 4 angstroms away from the center of the atoms of the ligand. Generally these distances are determined by computer as discussed herein and in McRee 1993, however distances can be determined manually once the three dimensional model is made. See also Wagner et al., Nature 378(6558):670-697 (1995) for stereochemical figures of -three dimensional models. More commonly, the atoms of the ligand and the atoms of interacting amino acids are 3 to 4 angstroms apart. The invention can be practiced by repeating steps I and 2 to refine the fit of the ligand to the LBD and to determine a better ligand, such as an agonist, partial agonist, antagonist or partial antagonist or SARM. The three dimensional model of AR can be represented in two dimensions to determine which amino acids contact the ligand and to select a position on the ligand for chemical modification and changing the interaction with a particular amino acid compared to that before chemical modification. The chemical modification may be made using a computer, manually using a two dimensional representation of the three dimensional model or by chemically synthesizing the ligand. The ligand can also interact with distant amino acids after chemical modification of the ligand to create a new ligand. Distant amino acids are generally not in contact with the ligand before chemical modification. A chemical modification can change the structure of the ligand to make as new ligand that interacts with a distant amino acid usually at least 4.5

angstroms away from the ligand, preferably wherein said first chemical moiety is 6 to 12 angstroms away from a distant amino acid. Often distant amino acids will not line the surface of the binding cavity for the ligand, they are too far away from the ligand to be part of a pocket or binding cavity. The interaction between a LBD amino acid and an atom of an LBD ligand can be made by any force or attraction described in nature. Usually the interaction between the atom of the amino acid and the ligand will be the result of a hydrogen bonding interaction, charge interaction, hydrophobic interaction, van der Waals interaction or dipole interaction. In the case of the hydrophobic interaction it is recognized that this is not a per se interaction between the amino acid and ligand, but rather the usual result, in part, of the repulsion of water or other hydrophilic group from a hydrophobic surface. Reducing or enhancing the interaction of the LBD and a ligand can be measured by calculating or testing binding energies, computationally or using thermodynamic or kinetic methods as known in the art.

Chemical modifications will often enhance or reduce interactions of an atom of a LBD amino acid and an atom of an LBD ligand. Steric hindrance will be a common means of changing the interaction of the LBD binding cavity with the activation domain.

The present invention also provides methods for identifying compounds that modulate androgen receptor activity. Various methods or combinations thereof can be used to identify these compounds. For example, test compounds can be modeled that fit spatially into the AR-LBD as defined by structure coordinates according to Table A, or using a three-dimensional structural model of AR-LBD, mutant AR-LBD or AR-LBD homolog or portion thereof. Structure coordinates of the ligand binding site, in particular amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 can also be used to identify structural and chemical features. Identified structural or chemical features can then be employed to design or select compounds as potential AR modulators. By structural and chemical

features it is meant to include, but is not limited to, van der Waals interactions, hydrogen bonding interactions, charge interaction, hydrophobic bonding interaction, hydrophobic interaction and dipole interaction. Alternatively, or in conjunction, the three-dimensional structural model or the ligand binding site can be employed to design or select compounds as potential AR modulators. Compounds identified as potential AR modulators can then be synthesized and screened in an assay characterized by binding of a test compound to the AR-LBD. Examples of assays useful in screening of potential AR modulators include, but are not limited to, screening in silico, *in vitro* assays and high throughput assays. Finally, these methods may also involve modifying or replacing one or more amino acids from AR-LBD such as V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD according to Table A.

A preferred method of the invention can be described as a computational method of designing an androgen receptor antagonist from an androgen receptor agonist comprising:

1) determining a structure of a molecular recognition domain of said agonist using a three dimensional model of a crystallized protein comprising an AR-LBD, and
2) selecting at least one chemical modification of said agonist that provides a ligand structure that extends beyond a binding site for said agonist and in the direction of at least one protein domain important in AR biological function.

Another preferred method of the invention can be described as a computational method of designing a selective androgen receptor modulator such as an androgen receptor super agonist or antagonist comprising:

1) determining at least one interacting amino acid of an AR-LBD that interacts with at least one first chemical moiety of said ligand using a three dimensional model of a crystallized protein comprising AR-LBD with a bound ligand, and

2) selecting at least one chemical modification of said first chemical moiety to produce a second chemical moiety with a structure to reduce or enhance an interaction between said interacting amino acid and said second chemical moiety compared to said interaction between said interacting amino acid and said first chemical moiety.

However, as will be understood by those of skill in the art upon this disclosure, other structure based design methods can be used. Various computational structure based design methods have been disclosed in the art.

For example, a number computer modeling systems are available in which the sequence of the AR-LBD and the AR-LBD structure (i.e., atomic coordinates of AR-LBD and/or the atomic coordinates of the active site, the bond and dihedral angles, and distances between atoms in the active site such as provided in Table A) can be input. This computer system then generates the structural details of the site in which a potential AR modulator binds so that complementary structural details of the potential modulators can be determined. Design in these modeling systems is generally based upon the compound being capable of physically and structurally associating with AR-LBD. In addition, the compound must be able to assume a conformation that allows it to associate with AR-LBD. Some modeling systems estimate the potential inhibitory or binding effect of a potential AR modulator prior to actual synthesis and testing.

Methods for screening chemical entities or fragments for their ability to associate with AR-LBD are also well known. Often these methods begin by visual inspection of the active site on the computer screen. Selected fragments or chemical entities are then positioned with the AR-LBD. Docking is accomplished using software such as QUANTA and SYBYL, following by energy minimization and molecular dynamics with standard molecular mechanic forcefields such as CHARMM and AMBER. Examples of computer programs which assist in the selection of chemical fragment or chemical entities useful in the present invention include, but are not limited to, GRID (Goodford , P.J. J. Med. Chem. 1985 28:849-857), AUTODOCK (Goodsell, D.S. and Olsen, A.J. Proteins,

Structure, Functions, and Genetics 1990 8:195-202), and DOCK (Kunts et al. J. Mol. Biol. 1982 161:269-288).

Upon selection of preferred chemical entities or fragments, their relationship to each other and AR-ABD can be visualized and the entities or fragments can be assembled into a single potential modulator. Programs useful in assembling the individual chemical entities include, but are not limited to CAVEAT (Bartlett et al. Molecular Recognition in Chemical and Biological Problems Special Publication, Royal Chem. Soc. 78, 182-196 (1989)) and 3D Database systems (Martin, Y.C. J. Med. Chem. 1992 35:2145-2154).

Alternatively, compounds may be designed *de novo* using either an empty active site or optionally including some portion of a known inhibitor. Methods of this type of design include, but are not limited to LUDI (Bohm H-J, J. Comp. Aid. Molec. Design 1992 6:61-78) and LeapFrog (Tripos Associates, St. Louis. MO).

The present invention is also directed to an AR-LBD selective androgen receptor modulator (SARM), in particular an agonist or antagonist or partial agonist or partial antagonist, identified by a computational process of the invention.

The present invention is further directed to a method for treating prostate cancer comprising administering an effective amount of an AR modulator, preferably an antagonist or partial antagonist, identified by a computational process of the invention.

The present invention is also direct to a method for treating an age related disease comprising administering an effective amount of an AR modulator, preferably an agonist or partial agonist, identified by a computational process of the invention, preferably wherein said age related disease is osteoporosis, muscle wasting or loss of libido.

Compounds identified as agonists, partial agonists, antagonists, partial antagonists or SARMs by the methods disclosed herein which are active when given orally can be formulated as liquids for example syrups, suspensions or emulsions, tablets, capsules and lozenges. A liquid composition will generally consist of a suspension or solution of the compound in a suitable liquid carrier(s), for example ethanol, glycerin, sorbitol, non-aqueous solvent such as polyethylene glycol, oils or water, with a suspending agent, preservative, surfactant, wetting agent,

flavoring or coloring agent. Alternatively, a liquid formulation can be prepared from a reconstitutable powder. For example a powder containing active compound, suspending agent, sucrose and a sweetener can be reconstituted with water to form a suspension; and a syrup can be prepared from a powder containing active ingredient, sucrose and a sweetener. A composition in the form of a tablet can be prepared using any suitable pharmaceutical carrier(s) routinely used for preparing solid compositions. Examples of such carriers include magnesium stearate, starch, lactose, sucrose, microcrystalline cellulose, binders, for example polyvinylpyrrolidone. The tablet can also be provided with a color film coating, or color included as part of the carrier(s). In addition, active compound can be formulated in a controlled release dosage form as a tablet comprising a hydrophilic or hydrophobic matrix. A composition in the form of a capsule can be prepared using routine encapsulation procedures, for example by incorporation of active compound and excipients into a hard gelatin capsule. Alternatively, a semi-solid matrix of active compound and high molecular weight polyethylene glycol can be prepared and filled into a hard gelatin capsule; or a solution of active compound in polyethylene glycol or a suspension in edible oil, for example liquid paraffin or fractionated coconut oil can be prepared and filled into a soft gelatin capsule. Compounds identified by the processes described herein which are active when given parenterally can be formulated for intramuscular or intravenous administration. A typical composition for intra-muscular administration will consist of a suspension or solution of active ingredient in an oil, for example arachis oil or sesame oil. A typical composition for intravenous administration will consist of a sterile isotonic aqueous solution containing, for example active ingredient, dextrose, sodium chloride, a co-solvent, for example polyethylene glycol and, optionally, a chelating agent, for example ethylenediaminetetracetic acid and an anti-oxidant, for example, sodium metabisulphite. Alternatively, the solution can be freeze dried and then reconstituted with a suitable solvent just prior to administration. Identified compounds which are active on rectal administration can be formulated as suppositories. A typical suppository formulation will generally consist of active ingredient with a binding and/or lubricating agent such as a gelatin or cocoa butter or other low

melting vegetable or synthetic wax or fat. Identified compounds which are active on topical administration can be formulated as transdermal compositions. Such compositions include, for example, a backing, active compound reservoir, a control membrane, liner and contact adhesive. The typical daily dose of a varies according to individual needs, the condition to be treated and with the route of administration. Suitable doses are in the general range of from 0.001 to 10 mg/kg bodyweight of the recipient per day.

The following examples are to illustrate the invention, but should not be interpreted as a limitation thereon.

Examples

Cloning, Expression and Purification of the Androgen Receptor Ligand-Binding Domain

The rat androgen receptor (rAR) ligand-binding domain (LBD) cDNA, from amino acid 646 to 901, was cloned from a rat prostate cDNA library (Clontech) by PCR. The primers used were CATATGATTGAAGGCTATGAATGTCAACCTATCTTT (SEQ ID NO:3) and TCACTGTGTGTGGAAATAGATGGG (SEQ ID NO:4). The rat AR LBD was expressed as a fusion protein driven by the T7 promoter of pET28b vector (Novagen) to include an N-terminal polyhistidine tag and a thrombin cleavage site. The replacement of T877 for A (the LNCaP mutation) in this rAR LBD expression construct was performed with the QuickChange Site-Directed Mutagenesis kit (STRATAGENE). Dihydrotestosterone (DHT) was included in the *E. coli* (BL21-DE3) fermentation medium at a concentration of 0.05 mM. Induction with 0.4 mM isopropyl-β-D-thiogalactopyranoside was allowed to proceed for 16 hours at 20°C in M9 minimal media supplemented with casamino acids (Difco) and trace minerals, and pellets were stored at -70 °C. A total of 6-9 mg of recombinant AR LBD was isolated from a 15 gram cell pellet following sonication and chromatography on a nickel-chelate resin. Polyhistidine-tagged AR LBD of approximately 90% purity eluted at 0.45 M imidazole in a gradient of 0.05-1.0 imidazole. This material was quantitatively cleaved at an engineered site for thrombin recognition, followed by chromatography on benzamidine sepharose (Pharmacia) to remove the serine protease, with a 70% recovery. The final sample containing the sequence Gly-Ser-His-Met at the N-terminus followed by

residues 646-901 of the rat (664 – 919 in the human) AR LBD protein, was concentrated for crystallography to 2 mg/ml in 20 mM Tris (pH 7.5), 0.5 M NaCl, 10% glycerol, 1 mM EDTA and 1 mM DTT.

The sequence of the rat Androgen Receptor LBD (AR), as cloned, with the secondary structural features marked. For comparison, the aligned sequence of the Progesterone Receptor LBD (PR) is given. Residues involved in androgen binding are marked (*). Residues which are disordered in the crystal structure are underlined. The AR sequence is SEQ ID NO:1. The PR sequence is SEQ ID NO: 2.

```
|-H1--|                  |----------H3------------------
660 GSHMIEGYECQPIFLNVLEAIEPGVVCAGHDNNQPDSFAALLSSLNELGE   AR
678     GQDIQLIPPLINLLMSIEPDVIYAGHDNTKPDTSSSLLTSLNQLGE   PR
                                                  **

    ----------|          |----------H4/5----------|
710 RQLVHVVKWAKALPGFRNLHVDDQMAVIQYSWMGLMVFAMGWRSFTNVNS   AR
724 RQLLSVVKWSKSLPGFRNLHIDDQITLIQYSWMSLMVFGLGWRSYKHVSG   PR
     *                                  *      *

      SSSS  SSS |-H6|       |-----H7-----|      |---H8--
760 RMLYFAPDLVFNEYRMHKSRMYSQCVRMRHLSQEFGWLQITPQEFLCMKA   AR
774 QMLYFAPDLILNEQRMKESSFYSLCLTMWQIPQEFVKLQVSQEEFLCMKV   PR

    -|   SSS        |------H9------|           |--------
810 LLLFSIIPVDGLKNQKFFDELRMNYIKELDRIIACKRKNPTSCSRRFYQL   AR
824 LLLLNTIPLEGLRSQTQFEEMRSSYIRELIKAIGLRQKGVVSSSQRFYQL   PR

    ---H10/11------------| |--|      |-----H12-----|
860 TKLLDSVQPIARELHQFTFDLLIKSHMVSVDFPEMMAEIISVQVPKILSG   AR
874 TKLLDNLHDLVKQLHLYCLNTFIQSRALSVEFPEMMSEVIAAQLPKILAG   PR
                      *

     SSS
910 KVKPIYFHTQ  AR
924 MVKPLLFHK   PR
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Crystallization

The AR-LBD - Dihydrotestosterone (DHT) complex was crystallized at 20° C by vapor diffusion in the hanging-drop mode. In the crystallization trials, the protein complex as obtained from MMB&B was used without any further purification. In the initial trial to obtain crystallization conditions, a sparse matrix crystallization screen was done with the Crystal Screens 1 and 2 (Hampton Research). For each crystallization trial, a 2 µl drop was prepared by mixing 1 µl of purified protein (1.9 mg ml^{-1}) with an equal volume of reservoir solution. The reservoir contained 1.0 ml of the precipitating solution. Small crystals were obtained in two days from six of the drops (table 1).

Table 1: Crystallization Conditions

Screen/#	Precipitating Solution	Result
1/16	1.5 M Li Sulfate, 0.1M Na Hepes, pH 7.5	Small r ds
1/29	0.8 M Na/K Tartrate, 0.1M Na Hepes, pH 7.5	Larger rods
1/30	2% v/v PEG 400, 2.0 M Am Sulfate, 0.1M Na Hepes, pH 7.5	Small cubes
2/20	1.6 M Mg Sulfate, 0.1M MES, pH 6.5	Small crystallites
2/32	1.6 M Am Sulfate, 0.1 M Na Cl, 0.1 M Hepes, pH 7.5	Small rods
2/42	12% v/v Glycerol, 1.5 M Am Sulfate, 0.1 M Tris, pH 8.5	Small rods

The largest single crystal, measuring 0.05 mm x 0.04 mm x 0.26mm, was obtained from Crystal Screen 1, solution # 29 (0.8 M Na/K Tartrate, 0.1M Na Hepes, pH 7.5). This crystal was subsequently used in the initial data collection run (as described below).

Optimization of the crystallization condition was done using a Cyperlab C-200 automated crystallization robotic workstation. A crystallization trial was performed using a 24-step linear gradient from 0.6 M to 1.26 M Na tartrate, 100 Mm Hepes, pH 7.5 (Note: The optimization screen used sodium rather than sodium/potassium tartrate). The largest, rod shaped crystal, with dimensions 0.09 mm x 0.09 mm x 0.20mm, was obtained at 0.887 M Na Tartrate. This crystal was used in the second data collection run (as described below).

Data Collection and Reduction

For the initial X-ray experiment, the crystal from the initial crystallization screen was flash cooled by dipping it in a cryoprotectant solution containing the precipitating solution (0.8 M Na/K Tartrate, 0.1M Na Hepes, pH 7.5) with 250mm NaCl and 20% Glycerol added and then placed it in a cold stream at 100° K.

For data set 1, X-ray diffraction data were collected with an R-Axis II imaging plate detector. The radiation was generated from a Rigaku RU-200 rotating at 5 kw power with a fine focus filament (0.3 x 3.0mm) was monchromated (Cu Kα) and intensified by focusing with Yale mirrors (Molecular Structure Corporation). The crystal diffracted to better than 2.4 Å resolution. Autoindexing and processing of the measured intensity data was carried out with the HKL software package (Otwinoski, L. (1993) in CCP4 Study Weekend, Data Collection and

Processing (Sawyer,L., Issacs, N., and Bailey, S., Eds.) pp 56-62, SERC Daresbury Laboratory, Warrington, U.K). X-ray diffraction from the crystals have the symmetry and systematic absences of the orthorhombic space group P212121 with unit cell dimensions a = 56.03 Å , b = 66.27 Å, c= 70.38 Å, and one molecule per asymmetric unit (Mathews Volume = 2.16 $Å^3$ Da^{-1}).

A second X-ray diffraction data set (data set 2) was collected at the IMCA-CAT beamline (sector 17ID) at the Advanced Photon Source synchrotron at Argonne, Il. The crystal from the optimization screen described above, was flash-cooled by placing it in the reservoir solution (0.877 M Na Tartrate, 0.1M Na Hepes, pH 7.5) with 250mm NaCl and 20% Glycerol added, and then placing it in a cold stream at 100° K. The data were collected with a Bruker 2x2 mosaic CCD detector. The crystal diffracted to better than 2.0 Å. Autoindexing and processing of the measured intensity data was carried out with the HKL2000 software package (Otwinoski, L. (1993) in CCP4 Study Weekend, Data Collection and Processing (Sawyer,L., Issacs, N., and Bailey, S., Eds.) pp 56-62, SERC Daresbury Laboratory, Warrington, U.K.). The data collection and processing statistics for both data sets are summarized in table 2.

Structure Determination (Molecular Replacement)

The structure was determined by the method of molecular replacement with the program AmoRe (Navaza, J. (1994) AmoRe: an automated package for molecular replacement. Acta Cryst. D50, 157-163). The Progesterone Receptor ligand binding domain (PR-LBD), which has 54% sequence identity and 76% sequence homology to AR-LBD, was used as the search model. The atomic coordinates of PR-LBD (Protein Data Bank reference code 1A28) by Williams & Sigler (Nature 1998 393, 391) were unmodified except for the removal of the ligand and solvent molecules. A second molecular replacement search was performed with a theoretical model for the AR-LBD provided by the MMS/CADD group (table 3). The PR-LBD structure gave a slightly better solution than the AR-model (1.7σ vs.1.3σ above background) and was used in the subsequent refinement, although both structures gave equivalent results with no molecular interpenetration.

Table 2: Data Collection and Processing

	Data Set I	Data Set II
Date	5/19/99	6/17/99
Source/Detector	Rigaku RU-200	IMCA/APS 17ID
Detector	R-axis II	Bruker 2x2
Wavelength	Cu Kα (1.54 Å)	1.00 Å
Frames	364	400
ΔΦ	0.5°	0.5°
Crystal to plate distance	150 mm	135 mm
Time/frame	20 min	1 sec
Number of Observations	209,891	416,207
Data Reduction Program	HKL	HKL2000
Unique reflections	10,824	18,308
Reflections Used	10,114	16,862
Resolution	2.4 Å (2.5-2.4 Å)	2.0 Å (2.1-2.0 Å)
Completeness	93.8% (71.6%)	92.6 % (73.0 %)
Multiplicity	6.3	7.3
Mosiacity	0.502	0.332
Rsym (on I)	4.2 % (17.5%)	10.1 % (25.6%)
Space Group	$P2_12_12_1$	$P2_12_12_1$
a	56.09 Å	56.08 Å
b	66.43 Å	65.76 Å
c	70.54 Å	70.51 Å
Wilson B-value	39.05 Å^2	29.26 Å^2

Values for data in the last resolution shell are given in parentheses

Table 3 : Molecular Replacement Statistics

Search Model:	Progesterone (PDB file 1A28)	AR Model
Program Used	AmoRe	AMoRe
Resolution Range	8.0 – 4.0 Å	8.0 – 4.0 Å
Radius of Integration	25 Å	25 Å
Number of Reflections	2.393	2,393
Number of Atoms	2,019	2,094
RF Correlation (2nd solution)	0.16 (0.12)	0.13 (0.11)
TF Correlation (2nd solution)	0.31 (0.20)	0.23 (0.14)
TF R-factor (2nd solution)	49.0% (52.7%)	52.1% (54.0%)
Rigid Body Correlation	0.34	0.28
Rigid Body R-factor	48.1%	50.4%

Structure Refinement

The structure was first refined with the initial 2.4 Å data set (2σ data, 9,818 reflections) by the method of simulated annealing with

program X-PLOR (Brünger, A.T., Kuriyan, J. & Karplus, J. (1987) "Crystallographic R-factor refinement by molecular dynamics", *Science* **235**: 458-460) in four cycles to an R-factor of 27.7%. Each refinement cycle consisted of a least-squares minimization, simulated annealing at 3000°, and individual isotropic B-factor refinement. The first cycle, with the Progesterone molecular replacement model unmodified for the sequence differences between AR and PR, gave an R-factor of 33.8%. The model was then rebuilt using the AR amino acid sequence and a second refinement cycle gave an R-factor of 29.6%. At this stage of the refinement, the DHT molecule could be clearly seen in the difference electron density map.

After each cycle, the structure was carefully examined using molecular computer graphics program Chain (Sack, John S. (1988) "CHAIN- A Crystallographic Modeling Program", *J. Mol. Graphics* **6:** 224-225) and modifications were made to the structure as needed. Several residues, from both the N- and C-termini of the molecule, which were not seen in the electron density maps were removed from the model. After the second cycle of refinement, the DHT was added to the model. Solvent molecules were added where there were 3σ peaks in both the 2Fo - Fc and Fo - Fc electron density maps and removed if their B-factor went above 60 Å^2 . After four cycles of X-PLOR refinement, a careful examination of the electron density showed the model to be much improved, although molecular refitting still needed to be done in some regions. The density is clear except for some of the loop regions, particularly the loop between helices I and II, which was also poorly modeled in the PR structure.

Table 4: Refinement Statistics (X-PLOR)

Part I: 2σ data (9,818 reflections) to 2.4 Å

Cycle 1	251 residues	No ligand	0 waters	R = 33.8 %
Cycle 2	248 residues	No ligand	0 waters	R = 29.6%
Cycle 3	247 residues	ligand	18 waters	R = 28.3 %
Cycle 4	246 residues	ligand	40 waters	R = 27.7%

Part II: 2σ data (15,067 reflections) to 2.0 Å

Cycle 5	246 residues	ligand	32 waters	R = 27.9 %
Cycle 6	246 residues	ligand	57 waters	R = 26.8 %

Cycle 7	246 residues	ligand	58 waters	R = 26.7 %
Cycle 8	246 residues	ligand	106 waters	R = 24.2%

At this stage of the refinement, the higher resolution data collected at the APS synchrotron became available. Four additional X-PLOR refinement cycles were performed with the 2.0 Å data set (2σ data, 15,067 reflections) following the same protocol. The final structure has an R-factor of 24.2% with a total of 106 solvent molecules. The final refinement statistics are presented in table 5.

Table 5: Final Refinement Parameters

Resolution Range	10.0 – 2.0 Å
Reflections	15,067
R-factor	24.2 %
R-free	31.2 %
# residues	246 (672-917)
# atoms	2118 (1991 atoms, 21 DHT, 106 waters)
RMS deviations	
bond lengths	0.014 Å
bind angles	1.594°
Improper angles	1.558°
Average B-factors	
Protein	25.02 Å^2
DHT	14.40 Å^2
Water	30.21 Å^2
Wilson B-factor	29.26 Å^2

Description of the Molecule

The structure of AR-LBD is complete from residues 671 through 917 for the wild-type and 672 to 918 for the LNCaP mutant. Analysis of the structures with program PROCHECK showed only minor exceptions to the allowed geometry. In the wild-type structure, the first six residues of the chain (664 - 670) are not seen in the electron density and are probably disordered. This leaves only one residue before the initial residue of the first α-helix (H1) in the wild-type structure, none in the LNCaP mutant structure. On the C-terminal end, the last two residues (918 - 919) are not seen in the electron density of the wild-type structure, but only the last is missing in the mutant. In addition, since the loop between helices 9 and 10 (residues 845-850) is not well defined, it has been modeled as poly-alanine.

Folding and Packing

As expected, the AR LBD has the same overall three-dimensional structure as those of the other nuclear hormone receptor LBDs. The molecule is folded into a "helical sandwich" consisting of 10 α-helices. There are four small pieces of beta strand, forming two short beta-sheets; one in the core of the molecule between helices 5 and 6 near the ligand binding site, and the other formed by the loop between helices 8 and 9 and the C-terminus. This latter sheet, also seen in the PR LBD structure, holds helix 12 in the closed, agonist conformation, close to and capping the ligand binding site.

Lack of Dimer Formation

Studies have indicated that the estrogen, progesterone, and androgen receptors all function as homodimers and that AR LBD forms dimers in solution. Thus it could be expected that the AR LBD domains might form homodimers in the crystal similar to those previously seen in the RXR-α and estrogen receptor (ER) LBD crystal structures. In the PR LBD structure, the two monomers in the asymmetric unit are related by a dyad, but the two-fold-symmetric configuration is strikingly different from that of the RXR and ER homodimers and the area buried in this configuration is much smaller than would be expected for stable dimer formation. In the AR LBD crystal, the ligand-binding domains are unmistakably monomeric, and there are no twofold axes relating domains. Moreover, the homodimer interaction seen in the structures of ER and RXR LBDs is not possible for the AR LBD, as the C-terminal tail is bound to the groove formed by helices 9 and 10, thereby obstructing the contact region between monomers in RXR and ER homodimers. Whether this observation reflects a non-dimeric state of the AR LBD in the functional AR dimer or is an artifact of the conditions used for AR LBD crystallization remains to be determined. It is noteworthy that the ER LBD constructs used for crystallization have been truncated to remove an analogous C-terminal extension.

Comparison with Progesterone Receptor

While there is only 55% sequence identity between AR LBD and PR LBD, there is a 77% sequence similarity, and as expected, the three-dimensional structures of these two LBDs are very similar with an r.m.s.

deviation of 1.3 Å between corresponding Cα atom positions. As with PR, AR LBD has no helix 2, but its helix 12 is longer than those of RXR or TR. In the case of AR, while helices 10 and 11 are nearly contiguous, there is a proline residue at position 868 that causes a kink between the two helices .

Comparison with theoretical AR model

The theoretical AR model obtained from MMS/CADD and the AR structure have an r.m.s. deviation of 1.29 Å for the 247 alpha carbons. More importantly, the hormone binding site is virtually identical with the exception of the side chains of Met 732(749), Leu 863(880), and Leu 864 (881) which are in different rotomers. This causes the binding cavity to be more compact in the AR structure. Also, there is a flip of the side chain of Asn 688(705) so that the ND2 atom is in position to make a hydrogen bond to the carbonyl off of the D-ring.

Table 6: Comparison of AR-LBD to PR-LBD and Theoretical model

	Calpha	Main	Side	Total
AR vs. Pr	1.22 (246)	1.27 (983)	1.80 (772)	1.53 (1,755)
AR vs. CADD	1.25 (246)	1.31 (983)	2.41(971)	1.93 (1,954)

Binding of Dihydrotestosterone

At the end of the molecular replacement procedure with the PR LBD structure without progesterone as search model, the largest piece of difference electron density, at approximately the 3σ level, was found at the progesterone-binding site. Replacing the bound progesterone agonist (which has a carboxyl group at the 17-position) with a model of d-hydrotestosterone (DHT, which has a hydroxyl group at the 17-position) produced an even better fit to the difference electron density, indicating that DHT binds to AR LBD in an almost identical fashion to the way progesterone binds to PR LBD. Both agonists interact with helices 3, 5, and 11 of their respective LBDs. Ring A, which is identical in the two steroids, makes similar interactions with the side chains of Q711, M745, R752 (Q725, M759, R766 in PR LBD), and a conserved water molecule. The interactions with ring C are also similar, with close contacts to the mainchain of L704 (L718 in PR LBD) and sidechain of N705 (N719 in PR LBD). The contact between C18 and the Oγ1 of T877 is unique to the wild-type AR LBD, as the corresponding cysteinyl side chain is pointed away from the steroid in the PR LBD structure.

Since progesterone and DHT differ in the substituent on ring D, it is expected that interactions with respective receptors will differ in this region. In the AR LBD structure, Nδ2 of N705 makes a hydrogen bond to the D-ring hydroxyl of DHT. A similar interaction could be made between progesterone and the PR LBD if there were a flip of both the steroid acetyl group and the side chain of N719. This would place the oxygen approximately 3.2 Å from the Nδ2 atom of Asn 719. The ligand contact surface area is slightly larger for progesterone in PR than for DHT in AR (483 vs. 448 Å^2) but they are both considerably smaller than the ligand contact surface area in TR (559 Å^2), PPARγ (583 Å^2), or the Vitamin D receptor (677 Å^2).

Figure 3 shows two orthogonal views of the omit electron density map of dihydrotestosterone (DHT) in the hormone-binding site of AR-LBD. There are hydrogen bonds between the steroid and the side chains of Arg 752 and Asn 705.

Table 7: Dihydrotestosterone Contacts (3.4 Å)

Hydrogen Bonds		
O3	Arg 752 Nh2	2.89 Å (2.77 A)
O3	Gln 711 Nε2	3.36 Å (3.20 A)
O20	Asn 705 Nδ2	2.80 Å (3.20 A)
O20	Thr 877 Oγ1	2.70 Å (N/A)
Possible Close Contacts		
C11	Leu 704 O	3.31 Å
C12	Asn 705 Nδ2	3.07 Å
C17	Asn 705 Nδ2	3.34 Å
C19	Met 745 Sδ	3.38 Å
C18	Thr 877 Oγ1	3.07 Å

Comparison with Progesterone binding

Comparison of the structure of DHT in the AR-LBD with the structure of progesterone in the PR-LBD (Williams, S.P. & Sigler, P.B. (1998) "Atomic Structure of Progesterone Complexed with its Receptor", Nature 393, 391) shows a similar mode of binding. Ring A, which is identical in the two steroids, makes similar interactions with the side chains of Q711, M745, R752, Q711 and a conserved water molecule (table 8). The interaction with ring C are also similar, with close

contacts to the mainchain of L704 and sidechain of N705. The contact from C18 to the Oγ1 of T877 is unique to AR-LBD, as the corresponding cysteine sidechain is pointed away from the steroid in the PR-LBD structure

Since progesterone and DHT differ in the substitution off of ring D, it is expected that there will be different interactions with the protein in this region. In the AR structure, the Nδ2 atom of Asn 705 makes hydrogen bond to the D-ring hydroxyl.

A similar interaction could be made in the PR if there were a flip of both the steroid carboxyl group and the side chain of N719. This would place the carboxyl oxygen approximately 3.2 A from the Nδ2 atom of Asn 719. In AR-LBD, there is also a close contact to the side chain of T877 which is absent in the PR-LBD structure.

Figure 4 shows comparison of AR and PR steroid binding Comparison of the binding of dihydrotestosterone to AR-LBD (top) and of progesterone to PR-LBD (bottom). Note that an additional hydrogen bond interaction would be possible if both the sidechains of both N719 and the progesterone were flipped.

Table 8: Comparison of AR and PR steroid binding

	AR	PR
Ring A		
O3:	H-bond to R752 NH2 (2.9 A)	H-bond to R766 NH2 (2.8 A)
	H-bond to water (3.5 A)	H-bond to water (3.1 / 3.4 A)
	SC of Q711 in different rotomer distance to O3 is 3.4 and 4.13 A	Contact to SC of Gln 725 distance to O3 is 3.2 and 3.3 A
C19	Contact to M745 SD (3.4 A)	Similar orientation (3.5 A)
C2:	SC of Q711 (3.5 A)	different rotomer (3.2 & 3.3) distance to C4 is 4.1 A
Ring C		
C11	LO704 O (3.3A)	(3.5A)
C12	Contact to N705 Nδ2 (3.1A)	Contact to N719 Oδ1 (3.4 A)
C18	Contact T877 Oγ1 (3.1 A)	SC of C891 pointing away distance to Sγ is 3.8 A
Ring D		
O20/C21	O21 in AR is close to C21 in PR (Possible flip of Carboxyl in PR?)	

		N/A	O20: Contact to C891 Ca (3.2 A)
		O20: H-bond N705 Nδ2 (2.8A) O20: Contact T877 Cγ1 (2.7 A)	C21: Contact to N719 OD1 (3.2 A) SC of C891 pointing away
	C17	Contact N705 Nδ2 (3.3 A)	Ring in slightly different orientation; distance to N719 Oδ1 is 4.7 A

Structure of the Complex of DHT with the LBD of the LNCaP Mutant

In the LNCaP mutant, T877 is replaced by an alanine residue. The mutant LBD structure has an r.m.s. deviation of 0.8 Å compared to the wild-type structure, close to the expected r.m.s. deviation due to the estimated errors in the coordinates. In particular, the binding of DHT is essentially identical by wild-type and mutant LBDs except at the point of mutation. Here the replacement of T877 by alanine leaves additional space off the D-ring of DHT to accommodate a larger substituent on position 17. This may explain the promiscuous ability of the LNCaP mutant, unlike wild-type AR, to bind to a variety of other hormones and analogs like some progestins, estrogens and cortisols that differ from DHT in substitution at position 17. For example, the binding of flutamide, estradiol, and progesterone to the LNCaP mutant can activate the mutant receptor. Conversely, mutation of T877 to residues with larger sidechains such as aspartic acid and lysine would be expected completely preclude the binding of ligands with any substituent at position 17 of the D-ring and such mutations have been shown to totally eliminate androgen binding.

Table A

ATOM	1	CB	ILE	672	14.846	25.527	23.734	1.00	25.78
ATOM	2	CG2	ILE	672	16.247	25.008	24.099	1.00	25.56
ATOM	3	CG1	ILE	672	14.842	27.035	23.978	1.00	25.60
ATOM	4	CD1	ILE	672	15.312	27.404	25.360	1.00	25.81
ATOM	5	C	ILE	672	15.115	23.900	21.789	1.00	25.32
ATOM	6	O	ILE	672	16.189	23.926	21.195	1.00	24.67
ATOM	7	N	ILE	672	13.004	25.282	22.008	1.00	24.75
ATOM	8	CA	ILE	672	14.475	25.215	22.242	1.00	25.11
ATOM	9	N	PHE	673	14.448	22.768	22.030	1.00	25.89
ATOM	10	CA	PHE	673	14.980	21.446	21.635	1.00	25.86
ATOM	11	CB	PHE	673	14.020	20.306	22.029	1.00	26.22
ATOM	12	CG	PHE	673	14.557	18.923	21.722	1.00	25.12
ATOM	13	CD1	PHE	673	15.765	18.501	22.251	1.00	25.16
ATOM	14	CD2	PHE	673	13.877	18.066	20.874	1.00	25.81
ATOM	15	CE1	PHE	673	16.286	17.255	21.946	1.00	23.42
ATOM	16	CE2	PHE	673	14.403	16.809	20.567	1.00	25.08
ATOM	17	CZ	PHE	673	15.609	16.417	21.107	1.00	23.85
ATOM	18	C	PHE	673	15.213	21.374	20.147	1.00	25.25
ATOM	19	O	PHE	673	16.260	20.926	19.680	1.00	24.38
ATOM	20	N	LEU	674	14.193	21.792	19.412	1.00	25.01
ATOM	21	CA	LEU	674	14.237	21.802	17.969	1.00	25.58
ATOM	22	CB	LEU	674	12.833	21.974	17.391	1.00	26.05
ATOM	23	CG	LEU	674	12.067	20.653	17.317	1.00	26.55
ATOM	24	CD1	LEU	674	10.617	20.887	16.935	1.00	26.35
ATOM	25	CD2	LEU	674	12.762	19.758	16.304	1.00	26.09
ATOM	26	C	LEU	674	15.199	22.801	17.357	1.00	25.10
ATOM	27	O	LEU	674	15.743	22.518	16.294	1.00	26.08
ATOM	28	N	ASN	675	15.440	23.939	18.019	1.00	24.63
ATOM	29	CA	ASN	675	16.356	24.964	17.484	1.00	23.19
ATOM	30	CB	ASN	675	16.478	26.215	18.393	1.00	24.20
ATOM	31	CG	ASN	675	15.206	27.067	18.452	1.00	24.32
ATOM	32	OD1	ASN	675	14.368	27.062	17.547	1.00	24.82
ATOM	33	ND2	ASN	675	15.076	27.817	19.539	1.00	24.74
ATOM	34	C	ASN	675	17.726	24.338	17.397	1.00	21.66
ATOM	35	O	ASN	675	18.435	24.524	16.417	1.00	21.43
ATOM	36	N	VAL	676	18.095	23.612	18.448	1.00	21.17
ATOM	37	CA	VAL	676	19.394	22.952	18.507	1.00	20.92
ATOM	38	CB	VAL	676	19.718	22.442	19.934	1.00	21.33
ATOM	39	CG1	VAL	676	18.899	21.237	20.247	1.00	24.09
ATOM	40	CG2	VAL	676	21.192	22.095	20.065	1.00	21.88
ATOM	41	C	VAL	676	19.501	21.830	17.473	1.00	19.78
ATOM	42	O	VAL	676	20.421	21.827	16.646	1.00	19.99
ATOM	43	N	LEU	677	18.530	20.923	17.434	1.00	19.08
ATOM	44	CA	LEU	677	18.601	19.848	16.453	1.00	17.91
ATOM	45	CB	LEU	677	17.383	18.921	16.518	1.00	17.50
ATOM	46	CG	LEU	677	17.267	18.083	17.798	1.00	16.78
ATOM	47	CD1	LEU	677	16.355	16.934	17.541	1.00	17.01
ATOM	48	CD2	LEU	677	18.615	17.555	18.225	1.00	17.10
ATOM	49	C	LEU	677	18.768	20.427	15.068	1.00	16.96
ATOM	50	O	LEU	677	19.640	20.008	14.347	1.00	14.94
ATOM	51	N	GLU	678	17.980	21.445	14.736	1.00	19.12
ATOM	52	CA	GLU	678	18.058	22.121	13.437	1.00	20.06
ATOM	53	CB	GLU	678	16.972	23.188	13.317	1.00	23.33
ATOM	54	CG	GLU	678	15.532	22.646	13.381	1.00	28.64
ATOM	55	CD	GLU	678	14.459	23.736	13.387	1.00	32.31
ATOM	56	OE1	GLU	678	14.811	24.943	13.374	1.00	34.41
ATOM	57	OE2	GLU	678	13.253	23.384	13.410	1.00	34.91
ATOM	58	C	GLU	678	19.410	22.783	13.243	1.00	19.33

ATOM	59	O	GLU	678	19.966	22.737	12.152	1.00	18.20
ATOM	60	N	ALA	679	19.966	23.324	14.329	1.00	19.45
ATOM	61	CA	ALA	679	21.257	24.018	14.303	1.00	18.84
ATOM	62	CB	ALA	679	21.388	24.919	15.517	1.00	17.67
ATOM	63	C	ALA	679	22.472	23.094	14.195	1.00	19.25
ATOM	64	O	ALA	679	23.479	23.436	13.558	1.00	19.27
ATOM	65	N	ILE	680	22.395	21.914	14.802	1.00	18.82
ATOM	66	CA	ILE	680	23.518	20.984	14.742	1.00	17.49
ATOM	67	CB	ILE	680	23.674	20.231	16.056	1.00	17.05
ATOM	68	CG2	ILE	680	24.022	21.213	17.158	1.00	16.83
ATOM	69	CG1	ILE	680	22.393	19.467	16.391	1.00	15.55
ATOM	70	CD1	ILE	680	22.558	18.575	17.552	1.00	13.80
ATOM	71	C	ILE	680	23.516	19.984	13.593	1.00	16.89
ATOM	72	O	ILE	680	24.518	19.303	13.370	1.00	17.12
ATOM	73	N	GLU	681	22.415	19.922	12.847	1.00	16.79
ATOM	74	CA	GLU	681	22.265	19.002	11.719	1.00	17.26
ATOM	75	CB	GLU	681	20.902	19.227	11.094	1.00	16.72
ATOM	76	CG	GLU	681	20.579	18.300	9.952	1.00	18.48
ATOM	77	CD	GLU	681	20.473	16.823	10.348	1.00	17.51
ATOM	78	OE1	GLU	681	20.659	16.502	11.524	1.00	17.58
ATOM	79	OE2	GLU	681	20.214	15.981	9.467	1.00	18.59
ATOM	80	C	GLU	681	23.370	19.128	10.673	1.00	18.79
ATOM	81	O	GLU	681	23.517	20.173	10.043	1.00	20.09
ATOM	82	N	PRO	682	24.145	18.044	10.437	1.00	19.02
ATOM	83	CD	PRO	682	23.969	16.704	11.019	1.00	18.22
ATOM	84	CA	PRO	682	25.252	18.021	9.472	1.00	19.11
ATOM	85	CB	PRO	682	25.681	16.546	9.493	1.00	18.30
ATOM	86	CG	PRO	682	25.338	16.109	10.846	1.00	17.08
ATOM	87	C	PRO	682	24.912	18.475	8.057	1.00	19.76
ATOM	88	O	PRO	682	23.771	18.382	7.625	1.00	21.13
ATOM	89	N	GLY	683	25.901	18.995	7.339	1.00	20.64
ATOM	90	CA	GLY	683	25.665	19.422	5.972	1.00	21.67
ATOM	91	C	GLY	683	25.809	18.260	4.990	1.00	23.13
ATOM	92	O	GLY	683	25.595	17.108	5.355	1.00	23.47
ATOM	93	N	VAL	684	26.190	18.567	3.748	1.00	23.58
ATOM	94	CA	VAL	684	26.365	17.573	2.685	1.00	22.44
ATOM	95	CB	VAL	684	26.320	18.216	1.259	1.00	24.93
ATOM	96	CG1	VAL	684	26.217	17.130	0.183	1.00	24.57
ATOM	97	CG2	VAL	684	25.153	19.228	1.131	1.00	24.89
ATOM	98	C	VAL	684	27.725	16.934	2.811	1.00	20.64
ATOM	99	O	VAL	684	28.708	17.614	3.042	1.00	19.82
ATOM	100	N	VAL	685	27.778	15.631	2.585	1.00	19.05
ATOM	101	CA	VAL	685	29.012	14.878	2.665	1.00	17.89
ATOM	102	CB	VAL	685	28.955	13.857	3.867	1.00	17.81
ATOM	103	CG1	VAL	685	30.303	13.189	4.086	1.00	15.58
ATOM	104	CG2	VAL	685	28.527	14.556	5.147	1.00	16.27
ATOM	105	C	VAL	685	29.143	14.112	1.345	1.00	17.88
ATOM	106	O	VAL	685	28.238	13.367	0.969	1.00	18.33
ATOM	107	N	CYS	686	30.224	14.339	0.609	1.00	17.00
ATOM	108	CA	CYS	686	30.451	13.628	-0.650	1.00	17.52
ATOM	109	CB	CYS	686	31.101	14.534	-1.706	1.00	17.76
ATOM	110	SG	CYS	686	30.166	16.031	-2.147	1.00	21.38
ATOM	111	C	CYS	686	31.354	12.447	-0.327	1.00	16.97
ATOM	112	O	CYS	686	32.141	12.496	0.615	1.00	17.15
ATOM	113	N	ALA	687	31.183	11.360	-1.065	1.00	17.74
ATOM	114	CA	ALA	687	31.949	10.132	-0.836	1.00	17.57
ATOM	115	CB	ALA	687	31.161	8.929	-1.295	1.00	16.91
ATOM	116	C	ALA	687	33.277	10.161	-1.526	1.00	18.06
ATOM	117	O	ALA	687	34.185	9.431	-1.139	1.00	17.98
ATOM	118	N	GLY	688	33.370	11.023	-2.539	1.00	18.50
ATOM	119	CA	GLY	688	34.580	11.167	-3.326	1.00	19.16
ATOM	120	C	GLY	688	34.705	10.099	-4.388	1.00	19.90

ATOM	121	O	GLY	688	35.802	9.730	-4.771	1.00	20.86
ATOM	122	N	HIS	689	33.582	9.630	-4.907	1.00	20.92
ATOM	123	CA	HIS	689	33.577	8.576	-5.912	1.00	22.43
ATOM	124	CB	HIS	689	32.195	7.917	-5.900	1.00	22.00
ATOM	125	CG	HIS	689	32.046	6.775	-6.857	1.00	22.28
ATOM	126	CD2	HIS	689	32.782	5.656	-7.033	1.00	22.64
ATOM	127	ND1	HIS	689	31.040	6.724	-7.796	1.00	22.44
ATOM	128	CE1	HIS	689	31.166	5.627	-8.516	1.00	23.43
ATOM	129	NE2	HIS	689	32.219	4.960	-8.074	1.00	23.78
ATOM	130	C	HIS	689	33.923	9.063	-7.328	1.00	24.19
ATOM	131	O	HIS	689	33.511	10.145	-7.731	1.00	24.06
ATOM	132	N	ASP	690	34.719	8.296	-8.073	1.00	26.27
ATOM	133	CA	ASP	690	35.017	8.691	-9.447	1.00	28.86
ATOM	134	CB	ASP	690	36.330	8.096	-9.963	1.00	28.93
ATOM	135	CG	ASP	690	36.696	8.618	-11.361	1.00	30.03
ATOM	136	OD1	ASP	690	37.868	8.497	-11.764	1.00	31.23
ATOM	137	OD2	ASP	690	35.819	9.170	-12.061	1.00	29.72
ATOM	138	C	ASP	690	33.872	8.164	-10.286	1.00	30.15
ATOM	139	O	ASP	690	33.701	6.952	-10.409	1.00	30.46
ATOM	140	N	ASN	691	33.065	9.067	-10.832	1.00	32.35
ATOM	141	CA	ASN	691	31.933	8.660	-11.655	1.00	33.60
ATOM	142	CB	ASN	691	30.725	9.562	-11.416	1.00	32.74
ATOM	143	CG	ASN	691	30.079	9.313	-10.074	1.00	32.95
ATOM	144	OD1	ASN	691	29.187	8.474	-9.930	1.00	32.13
ATOM	145	ND2	ASN	691	30.547	10.024	-9.069	1.00	33.57
ATOM	146	C	ASN	691	32.284	8.608	-13.136	1.00	35.13
ATOM	147	O	ASN	691	31.419	8.733	-13.999	1.00	36.66
ATOM	148	N	ALA	692	33.565	8.471	-13.434	1.00	36.15
ATOM	149	CA	ALA	692	33.995	8.365	-14.819	1.00	37.44
ATOM	150	CB	ALA	692	35.148	9.328	-15.103	1.00	36.71
ATOM	151	C	ALA	692	34.425	6.913	-15.027	1.00	38.39
ATOM	152	O	ALA	692	34.414	6.406	-16.139	1.00	39.10
ATOM	153	N	GLN	693	34.757	6.241	-13.928	1.00	39.29
ATOM	154	CA	GLN	693	35.200	4.849	-13.942	1.00	40.00
ATOM	155	CB	GLN	693	36.131	4.577	-12.745	1.00	41.81
ATOM	156	CG	GLN	693	37.538	4.029	-13.110	1.00	44.34
ATOM	157	CD	GLN	693	38.420	5.017	-13.902	1.00	45.44
ATOM	158	OE1	GLN	693	39.378	5.587	-13.363	1.00	45.95
ATOM	159	NE2	GLN	693	38.115	5.193	-15.186	1.00	45.47
ATOM	160	C	GLN	693	33.988	3.939	-13.854	1.00	39.48
ATOM	161	O	GLN	693	32.997	4.298	-13.217	1.00	40.11
ATOM	162	N	PRO	694	34.055	2.743	-14.485	1.00	38.78
ATOM	163	CD	PRO	694	35.138	2.286	-15.375	1.00	38.88
ATOM	164	CA	PRO	694	32.970	1.762	-14.489	1.00	36.98
ATOM	165	CB	PRO	694	33.571	0.601	-15.265	1.00	37.17
ATOM	166	CG	PRO	694	34.432	1.271	-16.234	1.00	38.48
ATOM	167	C	PRO	694	32.575	1.304	-13.109	1.00	35.56
ATOM	168	O	PRO	694	33.411	1.198	-12.204	1.00	35.44
ATOM	169	N	ASP	695	31.289	1.022	-12.958	1.00	34.27
ATOM	170	CA	ASP	695	30.776	0.534	-11.698	1.00	32.38
ATOM	171	CB	ASP	695	29.251	0.518	-11.694	1.00	29.77
ATOM	172	CG	ASP	695	28.660	1.901	-11.608	1.00	28.80
ATOM	173	OD1	ASP	695	27.532	2.100	-12.089	1.00	27.09
ATOM	174	OD2	ASP	695	29.329	2.794	-11.057	1.00	28.72
ATOM	175	C	ASP	695	31.318	-0.868	-11.524	1.00	32.55
ATOM	176	O	ASP	695	31.237	-1.707	-12.429	1.00	33.50
ATOM	177	N	SER	696	32.025	-1.052	-10.424	1.00	31.71
ATOM	178	CA	SER	696	32.577	-2.333	-10.077	1.00	30.42
ATOM	179	CB	SER	696	34.064	-2.383	-10.425	1.00	30.43
ATOM	180	OG	SER	696	34.854	-1.589	-9.567	1.00	31.47
ATOM	181	C	SER	696	32.340	-2.445	-8.577	1.00	30.15
ATOM	182	O	SER	696	32.275	-1.418	-7.885	1.00	30.10

ATOM	183	N	PHE	697	32.104	-3.669	-8.099	1.00	28.48
ATOM	184	CA	PHE	697	31.890	-3.933	-6.679	1.00	26.74
ATOM	185	CB	PHE	697	31.982	-5.442	-6.423	1.00	25.46
ATOM	186	CG	PHE	697	31.781	-5.827	-4.989	1.00	24.31
ATOM	187	CD1	PHE	697	30.536	-5.722	-4.398	1.00	24.48
ATOM	188	CD2	PHE	697	32.845	-6.281	-4.220	1.00	24.78
ATOM	189	CE1	PHE	697	30.344	-6.063	-3.071	1.00	24.65
ATOM	190	CE2	PHE	697	32.659	-6.626	-2.886	1.00	24.77
ATOM	191	CZ	PHE	697	31.406	-6.512	-2.315	1.00	24.30
ATOM	192	C	PHE	697	32.956	-3.205	-5.846	1.00	26.76
ATOM	193	O	PHE	697	32.641	-2.393	-4.972	1.00	27.12
ATOM	194	N	ALA	698	34.219	-3.495	-6.140	1.00	25.86
ATOM	195	CA	ALA	698	35.351	-2.911	-5.436	1.00	24.97
ATOM	196	CB	ALA	698	36.596	-3.305	-6.131	1.00	25.52
ATOM	197	C	ALA	698	35.323	-1.402	-5.300	1.00	25.24
ATOM	198	O	ALA	698	35.559	-0.852	-4.216	1.00	24.99
ATOM	199	N	ALA	699	35.029	-0.737	-6.414	1.00	25.11
ATOM	200	CA	ALA	699	35.001	0.717	-6.490	1.00	23.76
ATOM	201	CB	ALA	699	34.845	1.156	-7.943	1.00	24.31
ATOM	202	C	ALA	699	33.873	1.281	-5.668	1.00	22.91
ATOM	203	O	ALA	699	34.084	2.133	-4.795	1.00	22.51
ATOM	204	N	LEU	700	32.682	0.770	-5.957	1.00	21.56
ATOM	205	CA	LEU	700	31.440	1.185	-5.314	1.00	20.84
ATOM	206	CB	LEU	700	30.274	0.397	-5.937	1.00	19.59
ATOM	207	CG	LEU	700	29.249	0.984	-6.911	1.00	18.78
ATOM	208	CD1	LEU	700	29.727	2.269	-7.529	1.00	18.69
ATOM	209	CD2	LEU	700	28.952	-0.015	-7.957	1.00	17.10
ATOM	210	C	LEU	700	31.456	0.977	-3.793	1.00	20.77
ATOM	211	O	LEU	700	30.891	1.765	-3.035	1.00	19.67
ATOM	212	N	LEU	701	32.103	-0.093	-3.350	1.00	20.77
ATOM	213	CA	LEU	701	32.147	-0.367	-1.941	1.00	20.58
ATOM	214	CB	LEU	701	32.099	-1.871	-1.670	1.00	19.52
ATOM	215	CG	LEU	701	30.582	-2.050	-1.567	1.00	19.40
ATOM	216	CD1	LEU	701	30.046	-2.911	-2.642	1.00	17.73
ATOM	217	CD2	LEU	701	30.173	-2.510	-0.217	1.00	17.25
ATOM	218	C	LEU	701	33.261	0.365	-1.241	1.00	20.86
ATOM	219	O	LEU	701	33.126	0.734	-0.088	1.00	21.69
ATOM	220	N	SER	702	34.356	0.615	-1.937	1.00	21.06
ATOM	221	CA	SER	702	35.406	1.378	-1.316	1.00	20.96
ATOM	222	CB	SER	702	36.632	1.400	-2.190	1.00	21.52
ATOM	223	OG	SER	702	37.204	0.120	-2.175	1.00	23.71
ATOM	224	C	SER	702	34.874	2.791	-1.105	1.00	20.81
ATOM	225	O	SER	702	35.187	3.423	-0.103	1.00	20.82
ATOM	226	N	SER	703	34.023	3.250	-2.028	1.00	20.55
ATOM	227	CA	SER	703	33.443	4.585	-1.934	1.00	18.91
ATOM	228	CB	SER	703	32.755	4.966	-3.224	1.00	18.44
ATOM	229	OG	SER	703	33.748	5.182	-4.194	1.00	20.63
ATOM	230	C	SER	703	32.470	4.678	-0.793	1.00	18.35
ATOM	231	O	SER	703	32.520	5.625	-0.025	1.00	18.89
ATOM	232	N	LEU	704	31.596	3.684	-0.662	1.00	17.26
ATOM	233	CA	LEU	704	30.639	3.687	0.432	1.00	16.37
ATOM	234	CB	LEU	704	29.691	2.497	0.342	1.00	15.19
ATOM	235	CG	LEU	704	28.558	2.583	-0.660	1.00	14.03
ATOM	236	CD1	LEU	704	27.882	1.259	-0.748	1.00	12.28
ATOM	237	CD2	LEU	704	27.582	3.681	-0.235	1.00	14.48
ATOM	238	C	LEU	704	31.366	3.678	1.761	1.00	16.10
ATOM	239	O	LEU	704	30.925	4.340	2.696	1.00	16.81
ATOM	240	N	ASN	705	32.495	2.961	1.829	1.00	16.70
ATOM	241	CA	ASN	705	33.307	2.863	3.049	1.00	16.66
ATOM	242	CB	ASN	705	34.398	1.794	2.924	1.00	15.46
ATOM	243	CG	ASN	705	33.850	0.384	2.941	1.00	16.24
ATOM	244	OD1	ASN	705	34.448	-0.512	2.385	1.00	16.82

ATOM	245	ND2	ASN	705	32.726	0.180	3.592	1.00	16.07
ATOM	246	C	ASN	705	33.955	4.201	3.410	1.00	17.17
ATOM	247	O	ASN	705	33.970	4.587	4.570	1.00	17.46
ATOM	248	N	GLU	706	34.512	4.882	2.415	1.00	17.04
ATOM	249	CA	GLU	706	35.151	6.193	2.598	1.00	17.55
ATOM	250	CB	GLU	706	35.739	6.668	1.258	1.00	18.93
ATOM	251	CG	GLU	706	36.394	8.029	1.282	1.00	21.19
ATOM	252	CD	GLU	706	37.488	8.146	2.347	1.00	23.68
ATOM	253	OE1	GLU	706	37.586	9.225	2.978	1.00	25.14
ATOM	254	OE2	GLU	706	38.246	7.175	2.569	1.00	24.37
ATOM	255	C	GLU	706	34.089	7.180	3.069	1.00	16.10
ATOM	256	O	GLU	706	34.313	8.023	3.950	1.00	16.62
ATOM	257	N	LEU	707	32.927	7.076	2.445	1.00	15.13
ATOM	258	CA	LEU	707	31.803	7.916	2.792	1.00	14.21
ATOM	259	CB	LEU	707	30.604	7.579	1.925	1.00	12.85
ATOM	260	CG	LEU	707	29.318	8.262	2.328	1.00	12.03
ATOM	261	CD1	LEU	707	29.537	9.745	2.280	1.00	13.09
ATOM	262	CD2	LEU	707	28.252	7.889	1.374	1.00	12.74
ATOM	263	C	LEU	707	31.461	7.634	4.228	1.00	14.91
ATOM	264	O	LEU	707	31.121	8.557	4.980	1.00	15.85
ATOM	265	N	GLY	708	31.532	6.358	4.602	1.00	13.93
ATOM	266	CA	GLY	708	31.230	5.976	5.965	1.00	12.96
ATOM	267	C	GLY	708	32.213	6.620	6.917	1.00	13.13
ATOM	268	O	GLY	708	31.849	7.061	7.987	1.00	13.55
ATOM	269	N	GLU	709	33.468	6.687	6.514	1.00	14.14
ATOM	270	CA	GLU	709	34.525	7.279	7.322	1.00	15.83
ATOM	271	CB	GLU	709	35.874	7.046	6.658	1.00	16.73
ATOM	272	CG	GLU	709	37.051	7.547	7.446	1.00	18.68
ATOM	273	CD	GLU	709	37.573	6.514	8.401	1.00	21.63
ATOM	274	OE1	GLU	709	36.766	5.660	8.826	1.00	23.39
ATOM	275	OE2	GLU	709	38.784	6.544	8.723	1.00	23.17
ATOM	276	C	GLU	709	34.334	8.775	7.486	1.00	16.65
ATOM	277	O	GLU	709	34.628	9.317	8.563	1.00	17.59
ATOM	278	N	ARG	710	33.845	9.427	6.428	1.00	16.70
ATOM	279	CA	ARG	710	33.616	10.869	6.418	1.00	17.32
ATOM	280	CB	ARG	710	33.459	11.346	4.990	1.00	16.07
ATOM	281	CG	ARG	710	34.659	11.098	4.137	1.00	16.18
ATOM	282	CD	ARG	710	34.329	11.498	2.706	1.00	16.39
ATOM	283	NE	ARG	710	35.512	11.535	1.850	1.00	15.28
ATOM	284	CZ	ARG	710	35.587	12.246	0.733	1.00	15.30
ATOM	285	NH1	ARG	710	34.550	12.975	0.357	1.00	14.96
ATOM	286	NH2	ARG	710	36.691	12.242	0.001	1.00	14.89
ATOM	287	C	ARG	710	32.376	11.230	7.218	1.00	17.85
ATOM	288	O	ARG	710	32.379	12.156	8.034	1.00	17.75
ATOM	289	N	GLN	711	31.291	10.516	6.955	1.00	18.71
ATOM	290	CA	GLN	711	30.067	10.745	7.697	1.00	19.38
ATOM	291	CB	GLN	711	28.908	9.938	7.127	1.00	19.79
ATOM	292	CG	GLN	711	28.377	10.566	5.878	1.00	22.36
ATOM	293	CD	GLN	711	27.058	10.010	5.446	1.00	23.37
ATOM	294	OE1	GLN	711	26.758	9.932	4.244	1.00	25.35
ATOM	295	NE2	GLN	711	26.228	9.677	6.410	1.00	24.52
ATOM	296	C	GLN	711	30.209	10.494	9.188	1.00	19.48
ATOM	297	O	GLN	711	29.564	11.183	9.985	1.00	19.57
ATOM	298	N	LEU	712	31.043	9.529	9.571	1.00	18.76
ATOM	299	CA	LEU	712	31.259	9.227	10.984	1.00	19.20
ATOM	300	CB	LEU	712	32.163	8.008	11.157	1.00	20.55
ATOM	301	CG	LEU	712	32.522	7.607	12.590	1.00	21.95
ATOM	302	CD1	LEU	712	31.288	7.641	13.484	1.00	23.43
ATOM	303	CD2	LEU	712	33.132	6.223	12.586	1.00	22.57
ATOM	304	C	LEU	712	31.876	10.428	11.704	1.00	19.23
ATOM	305	O	LEU	712	31.507	10.743	12.834	1.00	17.65
ATOM	306	N	VAL	713	32.809	11.099	11.039	1.00	19.70

ATOM	307	CA	VAL	713	33.427	12.270	11.619	1.00	19.68
ATOM	308	CB	VAL	713	34.453	12.859	10.658	1.00	20.01
ATOM	309	CG1	VAL	713	34.722	14.292	11.001	1.00	21.16
ATOM	310	CG2	VAL	713	35.750	12.069	10.750	1.00	20.06
ATOM	311	C	VAL	713	32.328	13.277	11.990	1.00	19.53
ATOM	312	O	VAL	713	32.325	13.802	13.086	1.00	20.00
ATOM	313	N	HIS	714	31.330	13.434	11.128	1.00	19.20
ATOM	314	CA	HIS	714	30.215	14.356	11.358	1.00	19.47
ATOM	315	CB	HIS	714	29.498	14.658	10.038	1.00	20.77
ATOM	316	CG	HIS	714	30.331	15.410	9.058	1.00	21.60
ATOM	317	CD2	HIS	714	31.369	15.016	8.283	1.00	22.31
ATOM	318	ND1	HIS	714	30.131	16.744	8.784	1.00	22.32
ATOM	319	CE1	HIS	714	31.005	17.139	7.876	1.00	23.41
ATOM	320	NE2	HIS	714	31.768	16.113	7.557	1.00	23.22
ATOM	321	C	HIS	714	29.183	13.885	12.383	1.00	18.83
ATOM	322	O	HIS	714	28.497	14.701	13.005	1.00	18.73
ATOM	323	N	VAL	715	29.006	12.572	12.485	1.00	18.39
ATOM	324	CA	VAL	715	28.063	11.972	13.434	1.00	16.86
ATOM	325	CB	VAL	715	27.869	10.435	13.134	1.00	16.78
ATOM	326	CG1	VAL	715	27.037	9.756	14.197	1.00	17.10
ATOM	327	CG2	VAL	715	27.183	10.259	11.817	1.00	17.34
ATOM	328	C	VAL	715	28.667	12.166	14.817	1.00	15.60
ATOM	329	O	VAL	715	27.958	12.422	15.788	1.00	15.49
ATOM	330	N	VAL	716	29.986	12.077	14.913	1.00	15.13
ATOM	331	CA	VAL	716	30.622	12.250	16.205	1.00	15.01
ATOM	332	CB	VAL	716	32.136	11.885	16.158	1.00	14.93
ATOM	333	CG1	VAL	716	32.825	12.233	17.481	1.00	13.26
ATOM	334	CG2	VAL	716	32.310	10.373	15.870	1.00	14.26
ATOM	335	C	VAL	716	30.419	13.681	16.708	1.00	15.83
ATOM	336	O	VAL	716	30.129	13.883	17.887	1.00	16.61
ATOM	337	N	LYS	717	30.544	14.665	15.816	1.00	16.59
ATOM	338	CA	LYS	717	30.390	16.082	16.183	1.00	17.20
ATOM	339	CB	LYS	717	30.884	16.974	15.041	1.00	18.94
ATOM	340	CG	LYS	717	32.361	16.747	14.698	1.00	22.56
ATOM	341	CD	LYS	717	33.245	16.752	15.978	1.00	25.34
ATOM	342	CE	LYS	717	34.294	15.609	16.007	1.00	27.06
ATOM	343	NZ	LYS	717	34.709	15.195	17.410	1.00	27.21
ATOM	344	C	LYS	717	28.951	16.387	16.534	1.00	16.77
ATOM	345	O	LYS	717	28.658	16.931	17.593	1.00	18.49
ATOM	346	N	TRP	718	28.049	15.976	15.659	1.00	15.68
ATOM	347	CA	TRP	718	26.618	16.143	15.868	1.00	14.61
ATOM	348	CB	TRP	718	25.889	15.442	14.689	1.00	11.97
ATOM	349	CG	TRP	718	24.433	15.266	14.841	1.00	9.66
ATOM	350	CD2	TRP	718	23.757	14.069	15.254	1.00	10.28
ATOM	351	CE2	TRP	718	22.373	14.371	15.293	1.00	9.98
ATOM	352	CE3	TRP	718	24.176	12.778	15.612	1.00	10.09
ATOM	353	CD1	TRP	718	23.472	16.199	14.645	1.00	9.89
ATOM	354	NE1	TRP	718	22.228	15.688	14.918	1.00	8.38
ATOM	355	CZ2	TRP	718	21.394	13.419	15.663	1.00	9.00
ATOM	356	CZ3	TRP	718	23.201	11.835	15.980	1.00	8.20
ATOM	357	CH2	TRP	718	21.835	12.171	16.004	1.00	7.32
ATOM	358	C	TRP	718	26.200	15.562	17.261	1.00	15.34
ATOM	359	O	TRP	718	25.659	16.269	18.124	1.00	14.55
ATOM	360	N	ALA	719	26.468	14.272	17.464	1.00	16.10
ATOM	361	CA	ALA	719	26.143	13.559	18.683	1.00	15.03
ATOM	362	CB	ALA	719	26.796	12.184	18.657	1.00	13.59
ATOM	363	C	ALA	719	26.623	14.346	19.881	1.00	15.62
ATOM	364	O	ALA	719	25.857	14.646	20.785	1.00	15.85
ATOM	365	N	LYS	720	27.870	14.781	19.828	1.00	17.45
ATOM	366	CA	LYS	720	28.463	15.516	20.924	1.00	18.63
ATOM	367	CB	LYS	720	29.970	15.625	20.715	1.00	19.81
ATOM	368	CG	LYS	720	30.644	14.292	21.012	1.00	21.18

ATOM	369	CD	LYS	720	32.136	14.334	20.860	1.00	23.81
ATOM	370	CE	LYS	720	32.762	12.975	21.244	1.00	25.84
ATOM	371	NZ	LYS	720	32.729	12.661	22.708	1.00	26.70
ATOM	372	C	LYS	720	27.822	16.860	21.204	1.00	18.98
ATOM	373	O	LYS	720	27.921	17.377	22.321	1.00	19.86
ATOM	374	N	ALA	721	27.070	17.369	20.238	1.00	18.21
ATOM	375	CA	ALA	721	26.406	18.651	20.382	1.00	18.10
ATOM	376	CB	ALA	721	26.584	19.461	19.146	1.00	17.43
ATOM	377	C	ALA	721	24.941	18.492	20.675	1.00	18.80
ATOM	378	O	ALA	721	24.192	19.485	20.660	1.00	19.16
ATOM	379	N	LEU	722	24.518	17.247	20.904	1.00	19.00
ATOM	380	CA	LEU	722	23.119	16.912	21.207	1.00	19.60
ATOM	381	CB	LEU	722	22.955	15.395	21.119	1.00	19.45
ATOM	382	CG	LEU	722	21.855	14.771	20.271	1.00	19.62
ATOM	383	CD1	LEU	722	21.540	15.657	19.099	1.00	17.02
ATOM	384	CD2	LEU	722	22.298	13.382	19.815	1.00	17.38
ATOM	385	C	LEU	722	22.754	17.362	22.616	1.00	20.27
ATOM	386	O	LEU	722	23.521	17.125	23.549	1.00	21.72
ATOM	387	N	PRO	723	21.574	17.992	22.811	1.00	20.69
ATOM	388	CD	PRO	723	20.500	18.317	21.861	1.00	20.29
ATOM	389	CA	PRO	723	21.211	18.428	24.167	1.00	21.24
ATOM	390	CB	PRO	723	19.767	18.917	23.997	1.00	20.40
ATOM	391	CG	PRO	723	19.706	19.349	22.624	1.00	20.05
ATOM	392	C	PRO	723	21.266	17.287	25.195	1.00	21.66
ATOM	393	O	PRO	723	20.821	16.165	24.935	1.00	21.14
ATOM	394	N	GLY	724	21.800	17.588	26.369	1.00	22.02
ATOM	395	CA	GLY	724	21.874	16.598	27.416	1.00	22.29
ATOM	396	C	GLY	724	22.838	15.478	27.132	1.00	23.13
ATOM	397	O	GLY	724	23.076	14.658	28.004	1.00	23.78
ATOM	398	N	PHE	725	23.434	15.446	25.946	1.00	24.14
ATOM	399	CA	PHE	725	24.360	14.368	25.610	1.00	24.24
ATOM	400	CB	PHE	725	24.915	14.554	24.214	1.00	23.59
ATOM	401	CG	PHE	725	25.648	13.353	23.703	1.00	23.80
ATOM	402	CD1	PHE	725	24.944	12.239	23.260	1.00	22.83
ATOM	403	CD2	PHE	725	27.046	13.328	23.675	1.00	22.40
ATOM	404	CE1	PHE	725	25.623	11.130	22.804	1.00	22.77
ATOM	405	CE2	PHE	725	27.731	12.226	23.221	1.00	21.05
ATOM	406	CZ	PHE	725	27.025	11.123	22.784	1.00	22.31
ATOM	407	C	PHE	725	25.505	14.170	26.582	1.00	24.85
ATOM	408	O	PHE	725	25.873	13.028	26.863	1.00	23.79
ATOM	409	N	ARG	726	26.083	15.270	27.070	1.00	25.97
ATOM	410	CA	ARG	726	27.207	15.229	28.033	1.00	27.63
ATOM	411	CB	ARG	726	27.831	16.620	28.204	1.00	29.27
ATOM	412	CG	ARG	726	28.622	17.087	26.995	1.00	31.68
ATOM	413	CD	ARG	726	29.759	16.141	26.727	1.00	34.22
ATOM	414	NE	ARG	726	30.657	16.595	25.670	1.00	37.18
ATOM	415	CZ	ARG	726	31.872	16.090	25.464	1.00	38.28
ATOM	416	NH1	ARG	726	32.635	16.558	24.486	1.00	39.44
ATOM	417	NH2	ARG	726	32.329	15.109	26.232	1.00	38.78
ATOM	418	C	ARG	726	26.902	14.615	29.423	1.00	27.24
ATOM	419	O	ARG	726	27.797	14.449	30.253	1.00	27.08
ATOM	420	N	ASN	727	25.632	14.316	29.683	1.00	27.15
ATOM	421	CA	ASN	727	25.244	13.695	30.938	1.00	26.29
ATOM	422	CB	ASN	727	23.717	13.687	31.115	1.00	25.46
ATOM	423	CG	ASN	727	23.118	15.085	31.195	1.00	24.95
ATOM	424	OD1	ASN	727	21.947	15.277	30.893	1.00	24.88
ATOM	425	ND2	ASN	727	23.909	16.055	31.628	1.00	24.54
ATOM	426	C	ASN	727	25.750	12.261	30.934	1.00	26.17
ATOM	427	O	ASN	727	25.992	11.689	31.994	1.00	27.30
ATOM	428	N	LEU	728	25.895	11.673	29.749	1.00	25.64
ATOM	429	CA	LEU	728	26.362	10.289	29.625	1.00	25.16
ATOM	430	CB	LEU	728	26.191	9.759	28.190	1.00	22.98

ATOM	431	CG	LEU	728	24.859	9.711	27.448	1.00	20.68
ATOM	432	CD1	LEU	728	25.084	9.133	26.076	1.00	19.66
ATOM	433	CD2	LEU	728	23.856	8.883	28.203	1.00	19.79
ATOM	434	C	LEU	728	27.833	10.208	29.974	1.00	25.79
ATOM	435	O	LEU	728	28.571	11.157	29.739	1.00	25.15
ATOM	436	N	HIS	729	28.247	9.064	30.516	1.00	27.05
ATOM	437	CA	HIS	729	29.642	8.808	30.871	1.00	28.68
ATOM	438	CB	HIS	729	29.737	7.455	31.570	1.00	30.72
ATOM	439	CG	HIS	729	31.132	7.042	31.943	1.00	33.13
ATOM	440	CD2	HIS	729	32.276	6.978	31.218	1.00	33.50
ATOM	441	ND1	HIS	729	31.460	6.603	33.209	1.00	34.21
ATOM	442	CE1	HIS	729	32.744	6.293	33.247	1.00	34.64
ATOM	443	NE2	HIS	729	33.263	6.510	32.049	1.00	34.52
ATOM	444	C	HIS	729	30.450	8.772	29.577	1.00	29.25
ATOM	445	O	HIS	729	30.003	8.182	28.594	1.00	29.28
ATOM	446	N	VAL	730	31.681	9.295	29.625	1.00	30.21
ATOM	447	CA	VAL	730	32.592	9.365	28.465	1.00	31.02
ATOM	448	CB	VAL	730	34.036	9.793	28.898	1.00	32.08
ATOM	449	CG1	VAL	730	35.077	9.446	27.811	1.00	32.91
ATOM	450	CG2	VAL	730	34.074	11.284	29.176	1.00	31.86
ATOM	451	C	VAL	730	32.662	8.108	27.600	1.00	30.89
ATOM	452	O	VAL	730	32.704	8.192	26.371	1.00	30.40
ATOM	453	N	ASP	731	32.770	6.956	28.244	1.00	30.81
ATOM	454	CA	ASP	731	32.819	5.709	27.509	1.00	31.55
ATOM	455	CB	ASP	731	33.244	4.536	28.410	1.00	36.23
ATOM	456	CG	ASP	731	32.966	3.152	27.771	1.00	40.32
ATOM	457	OD1	ASP	731	31.837	2.619	27.974	1.00	42.21
ATOM	458	OD2	ASP	731	33.867	2.599	27.075	1.00	42.23
ATOM	459	C	ASP	731	31.474	5.425	26.889	1.00	28.94
ATOM	460	O	ASP	731	31.408	4.912	25.789	1.00	29.47
ATOM	461	N	ASP	732	30.403	5.760	27.587	1.00	26.17
ATOM	462	CA	ASP	732	29.079	5.510	27.057	1.00	24.53
ATOM	463	CB	ASP	732	28.024	5.711	28.119	1.00	24.04
ATOM	464	CG	ASP	732	28.073	4.654	29.186	1.00	23.64
ATOM	465	OD1	ASP	732	28.728	3.592	28.984	1.00	22.31
ATOM	466	OD2	ASP	732	27.444	4.904	30.231	1.00	23.89
ATOM	467	C	ASP	732	28.770	6.387	25.875	1.00	23.96
ATOM	468	O	ASP	732	28.030	5.982	24.981	1.00	22.56
ATOM	469	N	GLN	733	29.288	7.612	25.920	1.00	23.56
ATOM	470	CA	GLN	733	29.121	8.591	24.855	1.00	22.94
ATOM	471	CB	GLN	733	29.942	9.847	25.166	1.00	22.73
ATOM	472	CG	GLN	733	29.359	10.776	26.225	1.00	23.24
ATOM	473	CD	GLN	733	30.208	12.013	26.480	1.00	23.27
ATOM	474	OE1	GLN	733	30.018	12.696	27.477	1.00	24.33
ATOM	475	NE2	GLN	733	31.130	12.316	25.577	1.00	23.47
ATOM	476	C	GLN	733	29.636	7.997	23.557	1.00	23.20
ATOM	477	O	GLN	733	28.979	8.075	22.522	1.00	23.08
ATOM	478	N	MET	734	30.853	7.459	23.625	1.00	23.37
ATOM	479	CA	MET	734	31.545	6.832	22.508	1.00	24.31
ATOM	480	CB	MET	734	33.003	6.596	22.906	1.00	27.26
ATOM	481	CG	MET	734	33.749	5.604	22.047	1.00	31.61
ATOM	482	SD	MET	734	35.293	5.121	22.821	1.00	39.54
ATOM	483	CE	MET	734	34.884	3.401	23.387	1.00	37.92
ATOM	484	C	MET	734	30.902	5.510	22.077	1.00	23.31
ATOM	485	O	MET	734	30.732	5.247	20.884	1.00	23.35
ATOM	486	N	ALA	735	30.571	4.671	23.052	1.00	21.64
ATOM	487	CA	ALA	735	29.939	3.390	22.788	1.00	20.44
ATOM	488	CB	ALA	735	29.650	2.683	24.110	1.00	20.71
ATOM	489	C	ALA	735	28.644	3.570	22.013	1.00	19.23
ATOM	490	O	ALA	735	28.398	2.905	21.015	1.00	19.59
ATOM	491	N	VAL	736	27.799	4.460	22.501	1.00	18.69
ATOM	492	CA	VAL	736	26.516	4.734	21.877	1.00	17.76

ATOM	493	CB	VAL	736	25.742	5.771	22.760	1.00	18.30
ATOM	494	CG1	VAL	736	25.373	6.998	22.011	1.00	17.05
ATOM	495	CG2	VAL	736	24.544	5.118	23.420	1.00	17.25
ATOM	496	C	VAL	736	26.673	5.133	20.389	1.00	18.16
ATOM	497	O	VAL	736	25.962	4.614	19.512	1.00	17.42
ATOM	498	N	ILE	737	27.658	5.985	20.096	1.00	17.60
ATOM	499	CA	ILE	737	27.914	6.429	18.724	1.00	16.31
ATOM	500	CB	ILE	737	29.046	7.497	18.683	1.00	14.71
ATOM	501	CG2	ILE	737	29.476	7.772	17.272	1.00	14.05
ATOM	502	CG1	ILE	737	28.602	8.819	19.325	1.00	15.11
ATOM	503	CD1	ILE	737	29.769	9.804	19.618	1.00	12.32
ATOM	504	C	ILE	737	28.352	5.216	17.904	1.00	16.74
ATOM	505	O	ILE	737	27.853	4.982	16.812	1.00	16.09
ATOM	506	N	GLN	738	29.281	4.451	18.468	1.00	18.15
ATOM	507	CA	GLN	738	29.850	3.260	17.845	1.00	17.97
ATOM	508	CB	GLN	738	30.960	2.715	18.713	1.00	20.53
ATOM	509	CG	GLN	738	32.278	3.394	18.568	1.00	23.88
ATOM	510	CD	GLN	738	33.306	2.726	19.439	1.00	26.69
ATOM	511	OE1	GLN	738	33.027	2.390	20.593	1.00	29.30
ATOM	512	NE2	GLN	738	34.483	2.475	18.887	1.00	28.53
ATOM	513	C	GLN	738	28.904	2.111	17.548	1.00	16.76
ATOM	514	O	GLN	738	29.249	1.226	16.788	1.00	16.47
ATOM	515	N	TYR	739	27.792	2.029	18.260	1.00	16.39
ATOM	516	CA	TYR	739	26.819	0.983	17.995	1.00	16.41
ATOM	517	CB	TYR	739	26.174	0.448	19.285	1.00	15.99
ATOM	518	CG	TYR	739	27.130	-0.115	20.313	1.00	15.68
ATOM	519	CD1	TYR	739	28.251	-0.852	19.950	1.00	15.41
ATOM	520	CE1	TYR	739	29.151	-1.317	20.915	1.00	16.17
ATOM	521	CD2	TYR	739	26.925	0.131	21.656	1.00	16.49
ATOM	522	CE2	TYR	739	27.817	-0.321	22.624	1.00	17.09
ATOM	523	CZ	TYR	739	28.921	-1.040	22.253	1.00	16.83
ATOM	524	OH	TYR	739	29.787	-1.435	23.256	1.00	18.24
ATOM	525	C	TYR	739	25.721	1.527	17.100	1.00	16.45
ATOM	526	O	TYR	739	25.138	0.793	16.295	1.00	17.63
ATOM	527	N	SER	740	25.453	2.822	17.195	1.00	15.61
ATOM	528	CA	SER	740	24.384	3.404	16.403	1.00	15.61
ATOM	529	CB	SER	740	23.619	4.403	17.252	1.00	15.49
ATOM	530	OG	SER	740	24.512	5.421	17.682	1.00	18.39
ATOM	531	C	SER	740	24.697	4.054	15.060	1.00	14.87
ATOM	532	O	SER	740	23.778	4.451	14.376	1.00	15.75
ATOM	533	N	TRP	741	25.948	4.188	14.659	1.00	14.33
ATOM	534	CA	TRP	741	26.202	4.835	13.382	1.00	14.83
ATOM	535	CB	TRP	741	27.706	4.997	13.113	1.00	15.35
ATOM	536	CG	TRP	741	28.465	3.720	13.000	1.00	17.05
ATOM	537	CD2	TRP	741	28.765	2.987	11.800	1.00	17.91
ATOM	538	CE2	TRP	741	29.467	1.834	12.190	1.00	18.98
ATOM	539	CE3	TRP	741	28.505	3.193	10.434	1.00	18.66
ATOM	540	CD1	TRP	741	28.995	3.016	14.020	1.00	17.12
ATOM	541	NE1	TRP	741	29.592	1.878	13.551	1.00	19.60
ATOM	542	CZ2	TRP	741	29.915	0.876	11.266	1.00	18.79
ATOM	543	CZ3	TRP	741	28.949	2.240	9.509	1.00	17.91
ATOM	544	CH2	TRP	741	29.644	1.098	9.934	1.00	18.35
ATOM	545	C	TRP	741	25.471	4.246	12.166	1.00	15.12
ATOM	546	O	TRP	741	24.902	4.995	11.376	1.00	15.56
ATOM	547	N	MET	742	25.391	2.920	12.034	1.00	14.55
ATOM	548	CA	MET	742	24.723	2.339	10.870	1.00	12.90
ATOM	549	CB	MET	742	24.785	0.815	10.866	1.00	13.16
ATOM	550	CG	MET	742	24.219	0.185	9.597	1.00	12.17
ATOM	551	SD	MET	742	25.353	0.336	8.263	1.00	15.00
ATOM	552	CE	MET	742	26.462	-0.994	8.639	1.00	13.52
ATOM	553	C	MET	742	23.290	2.763	10.699	1.00	12.47
ATOM	554	O	MET	742	22.886	3.153	9.610	1.00	13.31

ATOM	555	N	GLY	743	22.497	2.656	11.748	1.00	12.12
ATOM	556	CA	GLY	743	21.102	3.057	11.663	1.00	11.81
ATOM	557	C	GLY	743	20.947	4.558	11.452	1.00	12.08
ATOM	558	O	GLY	743	20.022	5.009	10.768	1.00	11.88
ATOM	559	N	LEU	744	21.835	5.336	12.070	1.00	12.77
ATOM	560	CA	LEU	744	21.817	6.797	11.972	1.00	12.22
ATOM	561	CB	LEU	744	22.884	7.418	12.888	1.00	11.70
ATOM	562	CG	LEU	744	22.702	7.481	14.399	1.00	9.95
ATOM	563	CD1	LEU	744	23.967	8.075	14.954	1.00	9.77
ATOM	564	CD2	LEU	744	21.516	8.341	14.799	1.00	9.16
ATOM	565	C	LEU	744	22.087	7.258	10.563	1.00	12.20
ATOM	566	O	LEU	744	21.424	8.173	10.080	1.00	14.22
ATOM	567	N	MET	745	23.083	6.651	9.921	1.00	12.34
ATOM	568	CA	MET	745	23.466	6.991	8.541	1.00	11.39
ATOM	569	CB	MET	745	24.839	6.427	8.191	1.00	10.75
ATOM	570	CG	MET	745	25.961	6.948	9.076	1.00	8.86
ATOM	571	SD	MET	745	27.509	6.429	8.487	1.00	11.97
ATOM	572	CE	MET	745	28.579	6.939	9.717	1.00	9.84
ATOM	573	C	MET	745	22.462	6.498	7.508	1.00	12.29
ATOM	574	O	MET	745	22.234	7.155	6.495	1.00	10.62
ATOM	575	N	VAL	746	21.855	5.342	7.793	1.00	12.05
ATOM	576	CA	VAL	746	20.874	4.733	6.934	1.00	11.50
ATOM	577	CB	VAL	746	20.524	3.315	7.426	1.00	11.19
ATOM	578	CG1	VAL	746	19.245	2.852	6.811	1.00	10.17
ATOM	579	CG2	VAL	746	21.615	2.355	7.095	1.00	9.64
ATOM	580	C	VAL	746	19.605	5.565	6.942	1.00	12.13
ATOM	581	O	VAL	746	19.000	5.792	5.907	1.00	12.72
ATOM	582	N	PHE	747	19.227	6.051	8.117	1.00	12.64
ATOM	583	CA	PHE	747	18.014	6.857	8.304	1.00	12.63
ATOM	584	CB	PHE	747	17.763	7.031	9.800	1.00	11.19
ATOM	585	CG	PHE	747	16.411	7.542	10.126	1.00	10.00
ATOM	586	CD1	PHE	747	15.286	6.780	9.847	1.00	9.30
ATOM	587	CD2	PHE	747	16.253	8.798	10.700	1.00	7.79
ATOM	588	CE1	PHE	747	14.008	7.260	10.136	1.00	8.30
ATOM	589	CE2	PHE	747	14.996	9.293	10.993	1.00	6.75
ATOM	590	CZ	PHE	747	13.867	8.524	10.707	1.00	8.21
ATOM	591	C	PHE	747	18.137	8.241	7.621	1.00	13.26
ATOM	592	O	PHE	747	17.178	8.751	7.042	1.00	13.81
ATOM	593	N	ALA	748	19.298	8.873	7.740	1.00	12.46
ATOM	594	CA	ALA	748	19.513	10.172	7.119	1.00	12.97
ATOM	595	CB	ALA	748	20.749	10.808	7.648	1.00	11.50
ATOM	596	C	ALA	748	19.640	9.988	5.635	1.00	13.78
ATOM	597	O	ALA	748	19.226	10.850	4.882	1.00	14.44
ATOM	598	N	MET	749	20.209	8.864	5.204	1.00	14.54
ATOM	599	CA	MET	749	20.381	8.578	3.782	1.00	14.78
ATOM	600	CB	MET	749	21.241	7.331	3.607	1.00	15.28
ATOM	601	CG	MET	749	21.622	6.945	2.199	1.00	15.33
ATOM	602	SD	MET	749	20.315	6.246	1.193	1.00	18.79
ATOM	603	CE	MET	749	20.226	4.627	1.835	1.00	18.82
ATOM	604	C	MET	749	19.023	8.390	3.142	1.00	15.85
ATOM	605	O	MET	749	18.808	8.780	1.990	1.00	17.51
ATOM	606	N	GLY	750	18.088	7.829	3.895	1.00	16.02
ATOM	607	CA	GLY	750	16.748	7.618	3.384	1.00	16.34
ATOM	608	C	GLY	750	16.057	8.956	3.225	1.00	17.79
ATOM	609	O	GLY	750	15.263	9.135	2.289	1.00	19.00
ATOM	610	N	TRP	751	16.361	9.897	4.121	1.00	17.36
ATOM	611	CA	TRP	751	15.778	11.241	4.091	1.00	17.99
ATOM	612	CB	TRP	751	16.108	12.026	5.366	1.00	16.08
ATOM	613	CG	TRP	751	15.528	13.458	5.416	1.00	14.99
ATOM	614	CD2	TRP	751	14.151	13.821	5.617	1.00	13.68
ATOM	615	CE2	TRP	751	14.099	15.230	5.697	1.00	12.98
ATOM	616	CE3	TRP	751	12.967	13.090	5.743	1.00	14.14

ATOM	617	CD1	TRP	751	16.225	14.636	5.364	1.00	13.27
ATOM	618	NE1	TRP	751	15.375	15.705	5.538	1.00	12.27
ATOM	619	CZ2	TRP	751	12.907	15.926	5.899	1.00	14.74
ATOM	620	CZ3	TRP	751	11.775	13.780	5.942	1.00	14.63
ATOM	621	CH2	TRP	751	11.756	15.188	6.020	1.00	14.82
ATOM	622	C	TRP	751	16.266	11.995	2.857	1.00	18.41
ATOM	623	O	TRP	751	15.457	12.558	2.124	1.00	20.13
ATOM	624	N	ARG	752	17.569	11.971	2.607	1.00	19.13
ATOM	625	CA	ARG	752	18.150	12.616	1.431	1.00	19.06
ATOM	626	CB	ARG	752	19.644	12.380	1.389	1.00	18.53
ATOM	627	CG	ARG	752	20.370	12.908	2.567	1.00	18.25
ATOM	628	CD	ARG	752	21.870	12.901	2.317	1.00	17.24
ATOM	629	NE	ARG	752	22.467	11.573	2.298	1.00	14.94
ATOM	630	CZ	ARG	752	22.976	10.973	3.370	1.00	14.90
ATOM	631	NH1	ARG	752	22.928	11.561	4.554	1.00	14.75
ATOM	632	NH2	ARG	752	23.684	9.864	3.240	1.00	13.87
ATOM	633	C	ARG	752	17.572	12.077	0.138	1.00	20.27
ATOM	634	O	ARG	752	17.392	12.815	-0.828	1.00	20.66
ATOM	635	N	SER	753	17.391	10.761	0.083	1.00	22.00
ATOM	636	CA	SER	753	16.823	10.099	-1.093	1.00	22.25
ATOM	637	CB	SER	753	16.716	8.590	-0.879	1.00	20.25
ATOM	638	OG	SER	753	17.988	8.027	-0.687	1.00	19.78
ATOM	639	C	SER	753	15.434	10.635	-1.289	1.00	23.31
ATOM	640	O	SER	753	14.978	10.803	-2.409	1.00	23.88
ATOM	641	N	PHE	754	14.762	10.870	-0.173	1.00	24.76
ATOM	642	CA	PHE	754	13.405	11.375	-0.156	1.00	26.45
ATOM	643	CB	PHE	754	12.835	11.243	1.245	1.00	26.43
ATOM	644	CG	PHE	754	11.447	11.765	1.364	1.00	28.06
ATOM	645	CD1	PHE	754	10.407	11.168	0.654	1.00	28.69
ATOM	646	CD2	PHE	754	11.184	12.895	2.118	1.00	27.96
ATOM	647	CE1	PHE	754	9.126	11.703	0.687	1.00	29.47
ATOM	648	CE2	PHE	754	9.901	13.442	2.160	1.00	28.93
ATOM	649	CZ	PHE	754	8.876	12.849	1.445	1.00	29.47
ATOM	650	C	PHE	754	13.239	12.818	-0.630	1.00	27.47
ATOM	651	O	PHE	754	12.543	13.100	-1.614	1.00	26.87
ATOM	652	N	THR	755	13.823	13.732	0.125	1.00	29.01
ATOM	653	CA	THR	755	13.725	15.134	-0.190	1.00	30.83
ATOM	654	CB	THR	755	14.345	15.972	0.918	1.00	29.71
ATOM	655	OG1	THR	755	15.669	15.524	1.183	1.00	28.99
ATOM	656	CG2	THR	755	13.553	15.796	2.164	1.00	29.63
ATOM	657	C	THR	755	14.317	15.460	-1.552	1.00	32.57
ATOM	658	O	THR	755	13.841	16.358	-2.234	1.00	33.24
ATOM	659	N	ASN	756	15.262	14.639	-1.991	1.00	34.71
ATOM	660	CA	ASN	756	15.920	14.842	-3.273	1.00	36.48
ATOM	661	CB	ASN	756	17.417	14.562	-3.149	1.00	36.89
ATOM	662	CG	ASN	756	18.137	15.616	-2.344	1.00	37.02
ATOM	663	OD1	ASN	756	17.563	16.237	-1.456	1.00	39.11
ATOM	664	ND2	ASN	756	19.392	15.844	-2.668	1.00	37.24
ATOM	665	C	ASN	756	15.360	14.065	-4.457	1.00	37.88
ATOM	666	O	ASN	756	14.684	14.628	-5.313	1.00	39.57
ATOM	667	N	VAL	757	15.654	12.773	-4.518	1.00	38.99
ATOM	668	CA	VAL	757	15.210	11.948	-5.633	1.00	39.74
ATOM	669	CB	VAL	757	16.274	10.869	-5.971	1.00	39.96
ATOM	670	CG1	VAL	757	17.639	11.540	-6.170	1.00	40.00
ATOM	671	CG2	VAL	757	16.354	9.819	-4.871	1.00	39.28
ATOM	672	C	VAL	757	13.835	11.308	-5.456	1.00	39.95
ATOM	673	O	VAL	757	13.501	10.335	-6.134	1.00	40.19
ATOM	674	N	ASN	758	13.037	11.874	-4.559	1.00	40.46
ATOM	675	CA	ASN	758	11.699	11.374	-4.265	1.00	41.28
ATOM	676	CB	ASN	758	10.678	11.894	-5.288	1.00	43.82
ATOM	677	CG	ASN	758	10.257	13.331	-5.005	1.00	44.84
ATOM	678	OD1	ASN	758	11.097	14.199	-4.764	1.00	46.40

ATOM	679	ND2	ASN	758	8.953	13.576	-4.987	1.00	45.71
ATOM	680	C	ASN	758	11.622	9.858	-4.100	1.00	40.91
ATOM	681	O	ASN	758	10.592	9.229	-4.404	1.00	40.73
ATOM	682	N	SER	759	12.733	9.298	-3.612	1.00	40.04
ATOM	683	CA	SER	759	12.891	7.877	-3.326	1.00	38.71
ATOM	684	CB	SER	759	11.763	7.415	-2.395	1.00	37.53
ATOM	685	OG	SER	759	11.496	8.369	-1.378	1.00	34.26
ATOM	686	C	SER	759	13.027	6.921	-4.532	1.00	39.24
ATOM	687	O	SER	759	12.833	5.711	-4.382	1.00	39.20
ATOM	688	N	ARG	760	13.409	7.438	-5.704	1.00	39.12
ATOM	689	CA	ARG	760	13.564	6.589	-6.892	1.00	38.62
ATOM	690	CB	ARG	760	13.451	7.422	-8.171	1.00	40.63
ATOM	691	CG	ARG	760	13.598	6.577	-9.444	1.00	44.41
ATOM	692	CD	ARG	760	13.903	7.394	-10.715	1.00	46.97
ATOM	693	NE	ARG	760	14.534	6.544	-11.729	1.00	48.86
ATOM	694	CZ	ARG	760	13.875	5.797	-12.614	1.00	49.74
ATOM	695	NH1	ARG	760	12.542	5.795	-12.649	1.00	50.04
ATOM	696	NH2	ARG	760	14.553	4.969	-13.398	1.00	49.46
ATOM	697	C	ARG	760	14.897	5.840	-6.876	1.00	36.88
ATOM	698	O	ARG	760	15.024	4.741	-7.426	1.00	37.48
ATOM	699	N	MET	761	15.902	6.466	-6.275	1.00	34.87
ATOM	700	CA	MET	761	17.238	5.890	-6.159	1.00	32.21
ATOM	701	CB	MET	761	18.171	6.510	-7.194	1.00	33.77
ATOM	702	CG	MET	761	17.588	6.682	-8.571	1.00	36.10
ATOM	703	SD	MET	761	18.859	7.115	-9.788	1.00	40.36
ATOM	704	CE	MET	761	18.737	8.904	-9.809	1.00	38.10
ATOM	705	C	MET	761	17.738	6.242	-4.751	1.00	29.46
ATOM	706	O	MET	761	17.144	7.080	-4.075	1.00	28.57
ATOM	707	N	LEU	762	18.837	5.635	-4.319	1.00	26.78
ATOM	708	CA	LEU	762	19.382	5.905	-2.992	1.00	24.13
ATOM	709	CB	LEU	762	19.956	4.637	-2.393	1.00	24.05
ATOM	710	CG	LEU	762	18.957	3.502	-2.272	1.00	23.69
ATOM	711	CD1	LEU	762	19.615	2.272	-1.632	1.00	23.99
ATOM	712	CD2	LEU	762	17.788	4.011	-1.439	1.00	24.34
ATOM	713	C	LEU	762	20.458	6.968	-3.040	1.00	23.01
ATOM	714	O	LEU	762	21.537	6.726	-3.548	1.00	22.65
ATOM	715	N	TYR	763	20.162	8.132	-2.475	1.00	22.03
ATOM	716	CA	TYR	763	21.066	9.273	-2.450	1.00	20.69
ATOM	717	CB	TYR	763	20.250	10.540	-2.266	1.00	23.12
ATOM	718	CG	TYR	763	20.946	11.782	-2.730	1.00	25.58
ATOM	719	CD1	TYR	763	20.841	12.187	-4.052	1.00	26.87
ATOM	720	CE1	TYR	763	21.416	13.373	-4.492	1.00	28.03
ATOM	721	CD2	TYR	763	21.662	12.590	-1.841	1.00	26.77
ATOM	722	CE2	TYR	763	22.247	13.789	-2.272	1.00	28.35
ATOM	723	CZ	TYR	763	22.107	14.172	-3.604	1.00	28.85
ATOM	724	OH	TYR	763	22.595	15.379	-4.047	1.00	30.59
ATOM	725	C	TYR	763	22.068	9.173	-1.323	1.00	18.78
ATOM	726	O	TYR	763	21.910	9.828	-0.304	1.00	17.73
ATOM	727	N	PHE	764	23.128	8.401	-1.538	1.00	17.33
ATOM	728	CA	PHE	764	24.152	8.191	-0.533	1.00	16.94
ATOM	729	CB	PHE	764	25.086	7.078	-0.956	1.00	15.91
ATOM	730	CG	PHE	764	24.505	5.724	-0.807	1.00	16.79
ATOM	731	CD1	PHE	764	24.211	4.961	-1.908	1.00	16.06
ATOM	732	CD2	PHE	764	24.267	5.205	0.450	1.00	16.83
ATOM	733	CE1	PHE	764	23.691	3.692	-1.756	1.00	18.06
ATOM	734	CE2	PHE	764	23.748	3.941	0.606	1.00	18.27
ATOM	735	CZ	PHE	764	23.458	3.176	-0.496	1.00	17.80
ATOM	736	C	PHE	764	24.964	9.441	-0.375	1.00	17.39
ATOM	737	O	PHE	764	25.379	9.797	0.734	1.00	17.28
ATOM	738	N	ALA	765	25.224	10.084	-1.503	1.00	17.00
ATOM	739	CA	ALA	765	26.013	11.292	-1.525	1.00	16.32
ATOM	740	CB	ALA	765	27.479	10.957	-1.460	1.00	16.17

ATOM	741	C	ALA	765	25.674	11.913	-2.841	1.00	16.66
ATOM	742	O	ALA	765	25.051	11.267	-3.675	1.00	16.71
ATOM	743	N	PRO	766	26.016	13.196	-3.032	1.00	17.18
ATOM	744	CD	PRO	766	26.544	14.169	-2.064	1.00	15.41
ATOM	745	CA	PRO	766	25.703	13.846	-4.311	1.00	17.49
ATOM	746	CB	PRO	766	26.183	15.277	-4.077	1.00	17.30
ATOM	747	CG	PRO	766	26.002	15.451	-2.608	1.00	17.07
ATOM	748	C	PRO	766	26.429	13.161	-5.481	1.00	17.65
ATOM	749	O	PRO	766	25.923	13.099	-6.598	1.00	17.73
ATOM	750	N	ASP	767	27.578	12.569	-5.166	1.00	18.27
ATOM	751	CA	ASP	767	28.416	11.850	-6.115	1.00	18.49
ATOM	752	CB	ASP	767	29.877	12.312	-5.955	1.00	18.71
ATOM	753	CG	ASP	767	30.413	12.135	-4.525	1.00	19.47
ATOM	754	OD1	ASP	767	29.611	12.038	-3.569	1.00	20.31
ATOM	755	OD2	ASP	767	31.650	12.102	-4.348	1.00	19.04
ATOM	756	C	ASP	767	28.330	10.317	-5.981	1.00	17.79
ATOM	757	O	ASP	767	29.191	9.594	-6.476	1.00	18.69
ATOM	758	N	LEU	768	27.334	9.820	-5.267	1.00	18.04
ATOM	759	CA	LEU	768	27.164	8.379	-5.110	1.00	18.20
ATOM	760	CB	LEU	768	27.955	7.809	-3.914	1.00	17.47
ATOM	761	CG	LEU	768	28.032	6.263	-3.786	1.00	16.12
ATOM	762	CD1	LEU	768	28.641	5.671	-5.047	1.00	14.30
ATOM	763	CD2	LEU	768	28.850	5.846	-2.563	1.00	15.17
ATOM	764	C	LEU	768	25.690	8.129	-4.930	1.00	18.58
ATOM	765	O	LEU	768	25.184	8.068	-3.812	1.00	17.79
ATOM	766	N	VAL	769	24.979	8.156	-6.048	1.00	19.79
ATOM	767	CA	VAL	769	23.553	7.895	-6.035	1.00	20.42
ATOM	768	CB	VAL	769	22.709	9.142	-6.447	1.00	19.95
ATOM	769	CG1	VAL	769	23.571	10.190	-7.096	1.00	20.70
ATOM	770	CG2	VAL	769	21.537	8.757	-7.277	1.00	19.19
ATOM	771	C	VAL	769	23.373	6.609	-6.852	1.00	20.73
ATOM	772	O	VAL	769	23.873	6.467	-7.961	1.00	22.43
ATOM	773	N	PHE	770	22.871	5.604	-6.157	1.00	19.70
ATOM	774	CA	PHE	770	22.683	4.277	-6.681	1.00	19.29
ATOM	775	CB	PHE	770	22.596	3.263	-5.503	1.00	18.44
ATOM	776	CG	PHE	770	23.930	2.757	-4.996	1.00	16.41
ATOM	777	CD1	PHE	770	25.079	3.546	-5.053	1.00	14.52
ATOM	778	CD2	PHE	770	24.025	1.468	-4.459	1.00	14.96
ATOM	779	CE1	PHE	770	26.291	3.070	-4.588	1.00	13.39
ATOM	780	CE2	PHE	770	25.243	0.979	-3.983	1.00	13.90
ATOM	781	CZ	PHE	770	26.383	1.786	-4.050	1.00	13.96
ATOM	782	C	PHE	770	21.425	4.134	-7.473	1.00	19.41
ATOM	783	O	PHE	770	20.367	4.583	-7.054	1.00	19.74
ATOM	784	N	ASN	771	21.534	3.474	-8.611	1.00	20.33
ATOM	785	CA	ASN	771	20.363	3.157	-9.410	1.00	20.23
ATOM	786	CB	ASN	771	20.524	3.593	-10.864	1.00	19.33
ATOM	787	CG	ASN	771	21.883	3.304	-11.403	1.00	18.89
ATOM	788	OD1	ASN	771	22.574	2.408	-10.942	1.00	19.51
ATOM	789	ND2	ASN	771	22.289	4.069	-12.382	1.00	19.02
ATOM	790	C	ASN	771	20.278	1.636	-9.292	1.00	21.01
ATOM	791	O	ASN	771	21.129	1.013	-8.648	1.00	20.52
ATOM	792	N	GLU	772	19.258	1.043	-9.898	1.00	22.23
ATOM	793	CA	GLU	772	19.056	-0.393	-9.841	1.00	22.51
ATOM	794	CB	GLU	772	17.888	-0.799	-10.711	1.00	23.17
ATOM	795	CG	GLU	772	16.562	-0.455	-10.099	1.00	24.81
ATOM	796	CD	GLU	772	15.761	-1.672	-9.724	1.00	25.41
ATOM	797	OE1	GLU	772	14.624	-1.488	-9.252	1.00	25.33
ATOM	798	OE2	GLU	772	16.265	-2.803	-9.913	1.00	26.23
ATOM	799	C	GLU	772	20.282	-1.102	-10.303	1.00	22.96
ATOM	800	O	GLU	772	20.631	-2.148	-9.785	1.00	23.89
ATOM	801	N	TYR	773	20.961	-0.531	-11.276	1.00	22.51
ATOM	802	CA	TYR	773	22.158	-1.164	-11.748	1.00	22.55

ATOM	803	CB	TYR	773	22.640	-0.492	-13.018	1.00	22.84
ATOM	804	CG	TYR	773	23.825	-1.191	-13.593	1.00	22.80
ATOM	805	CD1	TYR	773	23.680	-2.384	-14.304	1.00	23.02
ATOM	806	CE1	TYR	773	24.791	-3.041	-14.837	1.00	23.77
ATOM	807	CD2	TYR	773	25.095	-0.671	-13.418	1.00	22.59
ATOM	808	CE2	TYR	773	26.198	-1.309	-13.938	1.00	24.43
ATOM	809	CZ	TYR	773	26.047	-2.491	-14.643	1.00	24.22
ATOM	810	OH	TYR	773	27.172	-3.094	-15.155	1.00	25.98
ATOM	811	C	TYR	773	23.254	-1.167	-10.680	1.00	23.17
ATOM	812	O	TYR	773	23.969	-2.170	-10.523	1.00	24.08
ATOM	813	N	ARG	774	23.432	-0.044	-9.982	1.00	22.85
ATOM	814	CA	ARG	774	24.427	0.047	-8.922	1.00	21.74
ATOM	815	CB	ARG	774	24.623	1.487	-8.494	1.00	22.23
ATOM	816	CG	ARG	774	26.026	1.952	-8.735	1.00	22.58
ATOM	817	CD	ARG	774	26.073	3.066	-9.756	1.00	23.92
ATOM	818	NE	ARG	774	26.048	4.383	-9.146	1.00	24.69
ATOM	819	CZ	ARG	774	26.961	5.328	-9.365	1.00	25.97
ATOM	820	NH1	ARG	774	27.982	5.111	-10.171	1.00	25.01
ATOM	821	NH2	ARG	774	26.837	6.509	-8.783	1.00	26.70
ATOM	822	C	ARG	774	23.976	-0.796	-7.743	1.00	21.36
ATOM	823	O	ARG	774	24.791	-1.386	-7.052	1.00	20.25
ATOM	824	N	MET	775	22.669	-0.854	-7.512	1.00	21.93
ATOM	825	CA	MET	775	22.136	-1.681	-6.439	1.00	23.85
ATOM	826	CB	MET	775	20.614	-1.582	-6.380	1.00	23.42
ATOM	827	CG	MET	775	20.121	-0.241	-5.955	1.00	23.46
ATOM	828	SD	MET	775	18.333	-0.199	-5.865	1.00	26.50
ATOM	829	CE	MET	775	17.909	1.086	-7.064	1.00	27.26
ATOM	830	C	MET	775	22.550	-3.136	-6.666	1.00	25.38
ATOM	831	O	MET	775	22.897	-3.832	-5.733	1.00	25.75
ATOM	832	N	HIS	776	22.507	-3.593	-7.912	1.00	27.39
ATOM	833	CA	HIS	776	22.891	-4.954	-8.262	1.00	28.41
ATOM	834	CB	HIS	776	22.418	-5.302	-9.684	1.00	29.01
ATOM	835	CG	HIS	776	22.639	-6.738	-10.067	1.00	30.57
ATOM	836	CD2	HIS	776	21.877	-7.843	-9.864	1.00	30.73
ATOM	837	ND1	HIS	776	23.764	-7.168	-10.739	1.00	30.81
ATOM	838	CE1	HIS	776	23.685	-8.475	-10.932	1.00	29.87
ATOM	839	NE2	HIS	776	22.551	-8.907	-10.411	1.00	29.53
ATOM	840	C	HIS	776	24.403	-5.065	-8.178	1.00	29.55
ATOM	841	O	HIS	776	24.923	-5.865	-7.414	1.00	30.12
ATOM	842	N	LYS	777	25.109	-4.283	-8.989	1.00	31.13
ATOM	843	CA	LYS	777	26.570	-4.290	-8.980	1.00	32.73
ATOM	844	CB	LYS	777	27.130	-3.481	-10.161	1.00	31.29
ATOM	845	CG	LYS	777	26.678	-3.948	-11.525	1.00	30.55
ATOM	846	CD	LYS	777	27.443	-5.163	-12.003	1.00	29.83
ATOM	847	CE	LYS	777	28.928	-4.856	-12.116	1.00	30.35
ATOM	848	NZ	LYS	777	29.631	-5.860	-12.983	1.00	30.53
ATOM	849	C	LYS	777	27.032	-3.655	-7.660	1.00	34.07
ATOM	850	O	LYS	777	27.382	-2.478	-7.611	1.00	36.43
ATOM	851	N	SER	778	26.995	-4.437	-6.596	1.00	33.74
ATOM	852	CA	SER	778	27.387	-4.013	-5.250	1.00	33.75
ATOM	853	CB	SER	778	26.593	-2.789	-4.769	1.00	33.69
ATOM	854	OG	SER	778	25.254	-3.122	-4.452	1.00	33.41
ATOM	855	C	SER	778	27.065	-5.204	-4.366	1.00	32.95
ATOM	856	O	SER	778	27.447	-5.260	-3.194	1.00	31.80
ATOM	857	N	ARG	779	26.344	-6.149	-4.974	1.00	32.09
ATOM	858	CA	ARG	779	25.926	-7.386	-4.347	1.00	31.15
ATOM	859	CB	ARG	779	27.161	-8.256	-4.071	1.00	30.74
ATOM	860	CG	ARG	779	28.065	-8.415	-5.299	1.00	28.19
ATOM	861	CD	ARG	779	29.338	-9.182	-4.997	1.00	26.90
ATOM	862	NE	ARG	779	30.284	-9.129	-6.117	1.00	26.55
ATOM	863	CZ	ARG	779	31.583	-9.401	-6.014	1.00	26.64
ATOM	864	NH1	ARG	779	32.091	-9.753	-4.846	1.00	27.87

ATOM	865	NH2	ARG	779	32.398	-9.234	-7.050	1.00	26.64
ATOM	866	C	ARG	779	25.128	-7.063	-3.084	1.00	30.75
ATOM	867	O	ARG	779	25.027	-7.880	-2.163	1.00	31.03
ATOM	868	N	MET	780	24.521	-5.875	-3.097	1.00	29.82
ATOM	869	CA	MET	780	23.721	-5.381	-1.990	1.00	29.36
ATOM	870	CB	MET	780	24.295	-4.068	-1.473	1.00	30.17
ATOM	871	CG	MET	780	25.194	-4.191	-0.277	1.00	30.12
ATOM	872	SD	MET	780	25.835	-2.592	0.168	1.00	31.24
ATOM	873	CE	MET	780	24.525	-1.995	1.114	1.00	31.13
ATOM	874	C	MET	780	22.262	-5.165	-2.331	1.00	29.21
ATOM	875	O	MET	780	21.542	-4.505	-1.566	1.00	29.43
ATOM	876	N	TYR	781	21.831	-5.638	-3.497	1.00	28.58
ATOM	877	CA	TYR	781	20.433	-5.498	-3.897	1.00	28.82
ATOM	878	CB	TYR	781	20.229	-5.985	-5.338	1.00	27.73
ATOM	879	CG	TYR	781	18.896	-5.604	-5.964	1.00	26.05
ATOM	880	CD1	TYR	781	18.847	-4.861	-7.140	1.00	25.95
ATOM	881	CE1	TYR	781	17.624	-4.510	-7.718	1.00	25.58
ATOM	882	CD2	TYR	781	17.686	-5.984	-5.382	1.00	25.08
ATOM	883	CE2	TYR	781	16.471	-5.643	-5.955	1.00	24.57
ATOM	884	CZ	TYR	781	16.446	-4.904	-7.115	1.00	24.77
ATOM	885	OH	TYR	781	15.238	-4.572	-7.668	1.00	24.60
ATOM	886	C	TYR	781	19.701	-6.393	-2.929	1.00	30.06
ATOM	887	O	TYR	781	19.984	-7.589	-2.856	1.00	32.08
ATOM	888	N	SER	782	18.730	-5.821	-2.235	1.00	30.74
ATOM	889	CA	SER	782	17.935	-6.500	-1.198	1.00	31.41
ATOM	890	CB	SER	782	18.551	-7.836	-0.726	1.00	32.82
ATOM	891	OG	SER	782	17.785	-8.438	0.308	1.00	35.91
ATOM	892	C	SER	782	18.027	-5.483	-0.070	1.00	30.50
ATOM	893	O	SER	782	17.044	-4.807	0.230	1.00	30.31
ATOM	894	N	GLN	783	19.242	-5.287	0.459	1.00	29.34
ATOM	895	CA	GLN	783	19.455	-4.314	1.522	1.00	28.01
ATOM	896	CB	GLN	783	20.900	-4.309	2.020	1.00	28.50
ATOM	897	CG	GLN	783	21.327	-5.532	2.805	1.00	29.62
ATOM	898	CD	GLN	783	21.790	-6.634	1.900	1.00	32.01
ATOM	899	OE1	GLN	783	21.486	-6.621	0.714	1.00	33.24
ATOM	900	NE2	GLN	783	22.547	-7.587	2.436	1.00	32.18
ATOM	901	C	GLN	783	19.089	-2.963	0.935	1.00	26.36
ATOM	902	O	GLN	783	18.342	-2.211	1.544	1.00	26.08
ATOM	903	N	CYS	784	19.538	-2.698	-0.290	1.00	25.49
ATOM	904	CA	CYS	784	19.212	-1.439	-0.956	1.00	24.45
ATOM	905	CB	CYS	784	19.951	-1.312	-2.294	1.00	22.82
ATOM	906	SG	CYS	784	21.746	-0.989	-2.120	1.00	18.24
ATOM	907	C	CYS	784	17.698	-1.290	-1.146	1.00	25.03
ATOM	908	O	CYS	784	17.155	-0.183	-1.044	1.00	25.67
ATOM	909	N	VAL	785	17.003	-2.406	-1.360	1.00	25.25
ATOM	910	CA	VAL	785	15.538	-2.399	-1.547	1.00	25.02
ATOM	911	CB	VAL	785	14.987	-3.826	-1.903	1.00	25.94
ATOM	912	CG1	VAL	785	13.457	-3.901	-1.710	1.00	26.21
ATOM	913	CG2	VAL	785	15.349	-4.195	-3.324	1.00	26.31
ATOM	914	C	VAL	785	14.864	-1.979	-0.257	1.00	23.91
ATOM	915	O	VAL	785	13.881	-1.259	-0.260	1.00	24.19
ATOM	916	N	ARG	786	15.402	-2.455	0.853	1.00	25.02
ATOM	917	CA	ARG	786	14.855	-2.158	2.165	1.00	25.39
ATOM	918	CB	ARG	786	15.468	-3.114	3.198	1.00	26.15
ATOM	919	CG	ARG	786	15.392	-4.591	2.748	1.00	28.30
ATOM	920	CD	ARG	786	15.314	-5.583	3.900	1.00	29.76
ATOM	921	NE	ARG	786	14.269	-5.206	4.851	1.00	32.39
ATOM	922	CZ	ARG	786	14.292	-5.475	6.157	1.00	32.41
ATOM	923	NH1	ARG	786	15.301	-6.153	6.701	1.00	32.09
ATOM	924	NH2	ARG	786	13.326	-5.001	6.932	1.00	33.31
ATOM	925	C	ARG	786	15.083	-0.679	2.520	1.00	24.71
ATOM	926	O	ARG	786	14.180	-0.001	3.030	1.00	25.52

ATOM	927	N	MET	787	16.246	-0.146	2.160	1.00	23.53
ATOM	928	CA	MET	787	16.548	1.252	2.463	1.00	22.11
ATOM	929	CB	MET	787	18.018	1.528	2.261	1.00	20.46
ATOM	930	CG	MET	787	18.883	0.925	3.314	1.00	17.04
ATOM	931	SD	MET	787	20.578	0.861	2.788	1.00	20.46
ATOM	932	CE	MET	787	21.285	1.969	3.729	1.00	20.07
ATOM	933	C	MET	787	15.736	2.173	1.588	1.00	23.39
ATOM	934	O	MET	787	15.387	3.281	1.997	1.00	24.11
ATOM	935	N	ARG	788	15.521	1.752	0.348	1.00	24.89
ATOM	936	CA	ARG	788	14.738	2.499	-0.625	1.00	26.29
ATOM	937	CB	ARG	788	14.833	1.790	-1.980	1.00	28.55
ATOM	938	CG	ARG	788	14.166	2.474	-3.174	1.00	32.52
ATOM	939	CD	ARG	788	14.217	1.541	-4.395	1.00	35.44
ATOM	940	NE	ARG	788	13.426	1.996	-5.540	1.00	39.11
ATOM	941	CZ	ARG	788	13.899	2.177	-6.783	1.00	41.32
ATOM	942	NH1	ARG	788	15.182	1.960	-7.081	1.00	41.94
ATOM	943	NH2	ARG	788	13.079	2.567	-7.754	1.00	41.48
ATOM	944	C	ARG	788	13.312	2.475	-0.090	1.00	26.13
ATOM	945	O	ARG	788	12.596	3.473	-0.146	1.00	26.50
ATOM	946	N	HIS	789	12.920	1.339	0.483	1.00	26.36
ATOM	947	CA	HIS	789	11.587	1.173	1.052	1.00	26.76
ATOM	948	CB	HIS	789	11.377	-0.287	1.479	1.00	29.07
ATOM	949	CG	HIS	789	9.970	-0.609	1.879	1.00	30.42
ATOM	950	CD2	HIS	789	8.890	-0.944	1.137	1.00	31.35
ATOM	951	ND1	HIS	789	9.538	-0.567	3.188	1.00	32.05
ATOM	952	CE1	HIS	789	8.249	-0.856	3.235	1.00	32.56
ATOM	953	NE2	HIS	789	7.831	-1.087	2.001	1.00	32.55
ATOM	954	C	HIS	789	11.369	2.133	2.231	1.00	26.08
ATOM	955	O	HIS	789	10.275	2.671	2.394	1.00	25.72
ATOM	956	N	LEU	790	12.413	2.318	3.048	1.00	25.92
ATOM	957	CA	LEU	790	12.433	3.234	4.218	1.00	25.41
ATOM	958	CB	LEU	790	13.811	3.216	4.887	1.00	23.94
ATOM	959	CG	LEU	790	14.039	3.400	6.383	1.00	23.32
ATOM	960	CD1	LEU	790	15.444	3.930	6.570	1.00	22.41
ATOM	961	CD2	LEU	790	13.047	4.324	7.014	1.00	23.17
ATOM	962	C	LEU	790	12.218	4.654	3.720	1.00	25.47
ATOM	963	O	LEU	790	11.359	5.380	4.216	1.00	25.06
ATOM	964	N	SER	791	13.040	5.056	2.757	1.00	25.60
ATOM	965	CA	SER	791	12.942	6.375	2.177	1.00	26.51
ATOM	966	CB	SER	791	13.851	6.446	0.973	1.00	28.35
ATOM	967	OG	SER	791	14.936	5.559	1.179	1.00	32.32
ATOM	968	C	SER	791	11.521	6.561	1.716	1.00	26.02
ATOM	969	O	SER	791	10.950	7.632	1.885	1.00	26.00
ATOM	970	N	GLN	792	10.964	5.505	1.122	1.00	26.31
ATOM	971	CA	GLN	792	9.600	5.526	0.610	1.00	26.32
ATOM	972	CB	GLN	792	9.237	4.200	-0.112	1.00	28.65
ATOM	973	CG	GLN	792	9.700	4.109	-1.603	1.00	30.43
ATOM	974	CD	GLN	792	9.421	2.749	-2.277	1.00	31.95
ATOM	975	OE1	GLN	792	8.479	2.607	-3.062	1.00	33.53
ATOM	976	NE2	GLN	792	10.273	1.764	-2.007	1.00	32.31
ATOM	977	C	GLN	792	8.629	5.836	1.721	1.00	24.88
ATOM	978	O	GLN	792	7.702	6.610	1.528	1.00	24.96
ATOM	979	N	GLU	793	8.886	5.301	2.907	1.00	23.72
ATOM	980	CA	GLU	793	8.014	5.550	4.051	1.00	22.89
ATOM	981	CB	GLU	793	8.460	4.728	5.273	1.00	23.65
ATOM	982	CG	GLU	793	8.555	3.199	5.055	1.00	25.18
ATOM	983	CD	GLU	793	7.383	2.406	5.651	1.00	27.08
ATOM	984	OE1	GLU	793	6.207	2.735	5.351	1.00	25.97
ATOM	985	OE2	GLU	793	7.648	1.450	6.433	1.00	28.69
ATOM	986	C	GLU	793	7.949	7.041	4.400	1.00	21.58
ATOM	987	O	GLU	793	6.903	7.530	4.764	1.00	21.52
ATOM	988	N	PHE	794	9.042	7.784	4.274	1.00	21.26

ATOM	989	CA	PHE	794	8.999	9.208	4.598	1.00	20.65
ATOM	990	CB	PHE	794	10.334	9.890	4.323	1.00	19.81
ATOM	991	CG	PHE	794	11.413	9.541	5.304	1.00	19.96
ATOM	992	CD1	PHE	794	11.226	9.728	6.662	1.00	20.01
ATOM	993	CD2	PHE	794	12.599	8.974	4.878	1.00	19.43
ATOM	994	CE1	PHE	794	12.206	9.347	7.566	1.00	19.86
ATOM	995	CE2	PHE	794	13.570	8.593	5.787	1.00	18.95
ATOM	996	CZ	PHE	794	13.374	8.777	7.118	1.00	19.37
ATOM	997	C	PHE	794	7.929	9.863	3.759	1.00	22.26
ATOM	998	O	PHE	794	7.387	10.906	4.138	1.00	22.19
ATOM	999	N	GLY	795	7.688	9.270	2.585	1.00	23.81
ATOM	1000	CA	GLY	795	6.676	9.750	1.662	1.00	25.46
ATOM	1001	C	GLY	795	5.309	9.232	2.037	1.00	26.19
ATOM	1002	O	GLY	795	4.414	10.002	2.345	1.00	27.46
ATOM	1003	N	TRP	796	5.181	7.912	2.081	1.00	27.45
ATOM	1004	CA	TRP	796	3.931	7.239	2.428	1.00	28.24
ATOM	1005	CB	TRP	796	4.135	5.697	2.542	1.00	27.71
ATOM	1006	CG	TRP	796	4.478	4.998	1.187	1.00	27.50
ATOM	1007	CD2	TRP	796	5.208	3.763	0.985	1.00	26.97
ATOM	1008	CE2	TRP	796	5.312	3.556	-0.417	1.00	26.72
ATOM	1009	CE3	TRP	796	5.777	2.816	1.845	1.00	25.52
ATOM	1010	CD1	TRP	796	4.177	5.460	-0.079	1.00	27.17
ATOM	1011	NE1	TRP	796	4.676	4.601	-1.035	1.00	27.59
ATOM	1012	CZ2	TRP	796	5.967	2.448	-0.970	1.00	25.70
ATOM	1013	CZ3	TRP	796	6.427	1.714	1.290	1.00	25.51
ATOM	1014	CH2	TRP	796	6.514	1.543	-0.106	1.00	25.42
ATOM	1015	C	TRP	796	3.345	7.826	3.706	1.00	29.13
ATOM	1016	O	TRP	796	2.132	8.026	3.801	1.00	29.87
ATOM	1017	N	LEU	797	4.223	8.212	4.632	1.00	29.96
ATOM	1018	CA	LEU	797	3.816	8.768	5.923	1.00	29.80
ATOM	1019	CB	LEU	797	4.692	8.223	7.061	1.00	28.43
ATOM	1020	CG	LEU	797	4.552	6.736	7.383	1.00	27.68
ATOM	1021	CD1	LEU	797	5.709	6.269	8.228	1.00	27.20
ATOM	1022	CD2	LEU	797	3.216	6.470	8.058	1.00	26.62
ATOM	1023	C	LEU	797	3.864	10.260	5.991	1.00	30.39
ATOM	1024	O	LEU	797	3.447	10.827	6.983	1.00	32.25
ATOM	1025	N	GLN	798	4.415	10.908	4.978	1.00	31.03
ATOM	1026	CA	GLN	798	4.518	12.360	5.005	1.00	30.93
ATOM	1027	CB	GLN	798	3.117	13.030	4.964	1.00	31.58
ATOM	1028	CG	GLN	798	2.253	12.757	3.701	1.00	32.86
ATOM	1029	CD	GLN	798	0.944	13.580	3.633	1.00	32.89
ATOM	1030	OE1	GLN	798	0.342	13.933	4.648	1.00	33.16
ATOM	1031	NE2	GLN	798	0.521	13.892	2.421	1.00	33.46
ATOM	1032	C	GLN	798	5.267	12.764	6.294	1.00	30.02
ATOM	1033	O	GLN	798	4.716	13.460	7.147	1.00	30.51
ATOM	1034	N	ILE	799	6.497	12.283	6.462	1.00	28.60
ATOM	1035	CA	ILE	799	7.277	12.634	7.648	1.00	27.76
ATOM	1036	CB	ILE	799	8.546	11.747	7.829	1.00	26.34
ATOM	1037	CG2	ILE	799	9.382	12.246	9.007	1.00	25.78
ATOM	1038	CG1	ILE	799	8.168	10.286	8.046	1.00	25.57
ATOM	1039	CD1	ILE	799	7.271	10.063	9.211	1.00	25.52
ATOM	1040	C	ILE	799	7.729	14.094	7.552	1.00	28.59
ATOM	1041	O	ILE	799	8.181	14.552	6.496	1.00	29.81
ATOM	1042	N	THR	800	7.610	14.790	8.678	1.00	28.71
ATOM	1043	CA	THR	800	7.967	16.197	8.874	1.00	28.68
ATOM	1044	CB	THR	800	7.202	16.718	10.142	1.00	29.24
ATOM	1045	OG1	THR	800	5.839	17.003	9.815	1.00	31.49
ATOM	1046	CG2	THR	800	7.824	17.925	10.746	1.00	29.69
ATOM	1047	C	THR	800	9.475	16.347	9.116	1.00	28.69
ATOM	1048	O	THR	800	10.069	15.510	9.796	1.00	29.15
ATOM	1049	N	PRO	801	10.116	17.407	8.565	1.00	28.18
ATOM	1050	CD	PRO	801	9.618	18.376	7.569	1.00	27.62

ATOM	1051	CA	PRO	801	11.555	17.600	8.780	1.00	27.74
ATOM	1052	CB	PRO	801	11.797	18.983	8.178	1.00	27.08
ATOM	1053	CG	PRO	801	10.908	18.956	7.002	1.00	26.58
ATOM	1054	C	PRO	801	11.907	17.570	10.271	1.00	27.38
ATOM	1055	O	PRO	801	12.981	17.101	10.666	1.00	27.75
ATOM	1056	N	GLN	802	10.982	18.045	11.095	1.00	27.01
ATOM	1057	CA	GLN	802	11.189	18.079	12.542	1.00	26.73
ATOM	1058	CB	GLN	802	10.316	19.162	13.192	1.00	28.09
ATOM	1059	CG	GLN	802	10.582	20.596	12.692	1.00	29.79
ATOM	1060	CD	GLN	802	9.997	20.900	11.303	1.00	30.48
ATOM	1061	OE1	GLN	802	8.948	20.381	10.918	1.00	30.36
ATOM	1062	NE2	GLN	802	10.660	21.782	10.571	1.00	30.57
ATOM	1063	C	GLN	802	10.968	16.715	13.219	1.00	24.81
ATOM	1064	O	GLN	802	11.599	16.415	14.222	1.00	24.41
ATOM	1065	N	GLU	803	10.064	15.904	12.669	1.00	23.52
ATOM	1066	CA	GLU	803	9.797	14.558	13.196	1.00	21.64
ATOM	1067	CB	GLU	803	8.632	13.897	12.459	1.00	20.29
ATOM	1068	CG	GLU	803	7.277	14.434	12.848	1.00	18.44
ATOM	1069	CD	GLU	803	6.147	13.786	12.119	1.00	17.84
ATOM	1070	OE1	GLU	803	6.308	13.392	10.958	1.00	18.19
ATOM	1071	OE2	GLU	803	5.065	13.680	12.704	1.00	19.88
ATOM	1072	C	GLU	803	11.067	13.784	12.923	1.00	21.04
ATOM	1073	O	GLU	803	11.537	13.042	13.777	1.00	20.89
ATOM	1074	N	PHE	804	11.612	14.001	11.722	1.00	19.87
ATOM	1075	CA	PHE	804	12.863	13.418	11.254	1.00	19.24
ATOM	1076	CB	PHE	804	13.144	13.867	9.822	1.00	17.23
ATOM	1077	CG	PHE	804	14.557	13.645	9.384	1.00	14.85
ATOM	1078	CD1	PHE	804	15.012	12.380	9.095	1.00	13.76
ATOM	1079	CD2	PHE	804	15.440	14.706	9.301	1.00	13.69
ATOM	1080	CE1	PHE	804	16.335	12.160	8.729	1.00	13.79
ATOM	1081	CE2	PHE	804	16.765	14.496	8.936	1.00	13.36
ATOM	1082	CZ	PHE	804	17.214	13.217	8.647	1.00	12.84
ATOM	1083	C	PHE	804	14.034	13.802	12.157	1.00	20.31
ATOM	1084	O	PHE	804	14.807	12.939	12.564	1.00	21.30
ATOM	1085	N	LEU	805	14.187	15.086	12.463	1.00	20.30
ATOM	1086	CA	LEU	805	15.271	15.503	13.339	1.00	20.09
ATOM	1087	CB	LEU	805	15.250	17.008	13.582	1.00	19.58
ATOM	1088	CG	LEU	805	15.552	17.834	12.330	1.00	20.47
ATOM	1089	CD1	LEU	805	15.704	19.281	12.707	1.00	19.84
ATOM	1090	CD2	LEU	805	16.816	17.343	11.670	1.00	19.41
ATOM	1091	C	LEU	805	15.172	14.767	14.651	1.00	19.83
ATOM	1092	O	LEU	805	16.142	14.205	15.106	1.00	20.77
ATOM	1093	N	CYS	806	13.980	14.719	15.223	1.00	20.17
ATOM	1094	CA	CYS	806	13.765	14.026	16.494	1.00	21.27
ATOM	1095	CB	CYS	806	12.372	14.332	17.078	1.00	22.13
ATOM	1096	SG	CYS	806	12.142	16.017	17.706	1.00	27.50
ATOM	1097	C	CYS	806	13.938	12.515	16.378	1.00	20.36
ATOM	1098	O	CYS	806	14.575	11.904	17.241	1.00	20.30
ATOM	1099	N	MET	807	13.348	11.903	15.350	1.00	19.67
ATOM	1100	CA	MET	807	13.491	10.458	15.160	1.00	18.10
ATOM	1101	CB	MET	807	12.668	9.944	13.989	1.00	17.25
ATOM	1102	CG	MET	807	11.195	9.877	14.279	1.00	16.70
ATOM	1103	SD	MET	807	10.377	9.142	12.911	1.00	19.42
ATOM	1104	CE	MET	807	10.144	10.560	11.908	1.00	16.21
ATOM	1105	C	MET	807	14.947	10.062	14.979	1.00	17.75
ATOM	1106	O	MET	807	15.371	9.038	15.490	1.00	18.41
ATOM	1107	N	LYS	808	15.712	10.871	14.257	1.00	17.31
ATOM	1108	CA	LYS	808	17.116	10.592	14.054	1.00	16.27
ATOM	1109	CB	LYS	808	17.729	11.514	12.994	1.00	15.01
ATOM	1110	CG	LYS	808	19.171	11.154	12.733	1.00	14.63
ATOM	1111	CD	LYS	808	19.679	11.569	11.371	1.00	15.42
ATOM	1112	CE	LYS	808	19.422	13.053	11.092	1.00	15.64

ATOM	1113	NZ	LYS	808	20.232	13.940	11.928	1.00	14.15
ATOM	1114	C	LYS	808	17.857	10.726	15.376	1.00	16.89
ATOM	1115	O	LYS	808	18.731	9.908	15.677	1.00	16.07
ATOM	1116	N	ALA	809	17.522	11.747	16.166	1.00	16.53
ATOM	1117	CA	ALA	809	18.175	11.931	17.461	1.00	17.68
ATOM	1118	CB	ALA	809	17.628	13.139	18.155	1.00	16.91
ATOM	1119	C	ALA	809	17.989	10.691	18.348	1.00	19.03
ATOM	1120	O	ALA	809	18.932	10.207	18.996	1.00	20.50
ATOM	1121	N	LEU	810	16.766	10.184	18.392	1.00	19.36
ATOM	1122	CA	LEU	810	16.459	9.011	19.186	1.00	18.99
ATOM	1123	CB	LEU	810	14.966	8.811	19.263	1.00	19.09
ATOM	1124	CG	LEU	810	14.406	9.020	20.651	1.00	20.20
ATOM	1125	CD1	LEU	810	12.954	8.606	20.594	1.00	21.29
ATOM	1126	CD2	LEU	810	15.176	8.199	21.674	1.00	18.75
ATOM	1127	C	LEU	810	17.116	7.716	18.722	1.00	18.88
ATOM	1128	O	LEU	810	17.213	6.780	19.509	1.00	20.78
ATOM	1129	N	LEU	811	17.537	7.636	17.456	1.00	17.63
ATOM	1130	CA	LEU	811	18.215	6.447	16.959	1.00	15.58
ATOM	1131	CB	LEU	811	18.346	6.456	15.438	1.00	14.70
ATOM	1132	CG	LEU	811	17.148	6.107	14.574	1.00	14.14
ATOM	1133	CD1	LEU	811	17.511	6.408	13.164	1.00	13.66
ATOM	1134	CD2	LEU	811	16.744	4.632	14.746	1.00	13.62
ATOM	1135	C	LEU	811	19.598	6.328	17.582	1.00	15.42
ATOM	1136	O	LEU	811	20.189	5.252	17.554	1.00	17.27
ATOM	1137	N	LEU	812	20.153	7.429	18.084	1.00	13.97
ATOM	1138	CA	LEU	812	21.455	7.373	18.734	1.00	12.94
ATOM	1139	CB	LEU	812	22.004	8.790	18.937	1.00	12.69
ATOM	1140	CG	LEU	812	23.342	8.893	19.670	1.00	12.03
ATOM	1141	CD1	LEU	812	24.488	8.422	18.802	1.00	12.16
ATOM	1142	CD2	LEU	812	23.559	10.325	20.037	1.00	13.12
ATOM	1143	C	LEU	812	21.330	6.658	20.098	1.00	12.97
ATOM	1144	O	LEU	812	22.282	6.118	20.629	1.00	12.99
ATOM	1145	N	PHE	813	20.136	6.681	20.662	1.00	13.55
ATOM	1146	CA	PHE	813	19.859	6.064	21.950	1.00	14.19
ATOM	1147	CB	PHE	813	19.137	7.088	22.821	1.00	15.20
ATOM	1148	CG	PHE	813	19.818	8.435	22.841	1.00	16.11
ATOM	1149	CD1	PHE	813	20.946	8.640	23.624	1.00	15.97
ATOM	1150	CD2	PHE	813	19.349	9.472	22.036	1.00	16.07
ATOM	1151	CE1	PHE	813	21.604	9.845	23.615	1.00	18.37
ATOM	1152	CE2	PHE	813	19.991	10.687	22.014	1.00	17.54
ATOM	1153	CZ	PHE	813	21.126	10.883	22.801	1.00	17.99
ATOM	1154	C	PHE	813	18.971	4.856	21.753	1.00	14.71
ATOM	1155	O	PHE	813	18.058	4.618	22.530	1.00	14.79
ATOM	1156	N	SER	814	19.255	4.082	20.709	1.00	16.09
ATOM	1157	CA	SER	814	18.453	2.917	20.369	1.00	15.96
ATOM	1158	CB	SER	814	17.697	3.172	19.062	1.00	15.79
ATOM	1159	OG	SER	814	16.640	4.087	19.274	1.00	15.51
ATOM	1160	C	SER	814	19.169	1.581	20.294	1.00	16.05
ATOM	1161	O	SER	814	18.610	0.620	19.779	1.00	17.02
ATOM	1162	N	ILE	815	20.395	1.498	20.779	1.00	16.07
ATOM	1163	CA	ILE	815	21.099	0.226	20.747	1.00	17.04
ATOM	1164	CB	ILE	815	21.620	-0.086	19.325	1.00	16.75
ATOM	1165	CG2	ILE	815	22.222	1.113	18.706	1.00	17.43
ATOM	1166	CG1	ILE	815	22.600	-1.245	19.341	1.00	17.01
ATOM	1167	CD1	ILE	815	22.915	-1.753	17.953	1.00	17.98
ATOM	1168	C	ILE	815	22.172	0.187	21.826	1.00	17.86
ATOM	1169	O	ILE	815	23.111	0.981	21.802	1.00	18.49
ATOM	1170	N	ILE	816	21.994	-0.700	22.809	1.00	18.25
ATOM	1171	CA	ILE	816	22.913	-0.804	23.947	1.00	18.91
ATOM	1172	CB	ILE	816	22.298	-0.099	25.178	1.00	19.07
ATOM	1173	CG2	ILE	816	22.175	1.378	24.921	1.00	17.73
ATOM	1174	CG1	ILE	816	20.939	-0.692	25.537	1.00	18.04

ATOM	1175	CD1	ILE	816	20.516	-0.346	26.933	1.00	17.73
ATOM	1176	C	ILE	816	23.302	-2.226	24.385	1.00	20.13
ATOM	1177	O	ILE	816	22.615	-3.184	24.040	1.00	20.43
ATOM	1178	N	PRO	817	24.392	-2.385	25.180	1.00	20.85
ATOM	1179	CD	PRO	817	25.303	-1.373	25.730	1.00	21.00
ATOM	1180	CA	PRO	817	24.805	-3.720	25.631	1.00	22.05
ATOM	1181	CB	PRO	817	26.016	-3.444	26.523	1.00	21.47
ATOM	1182	CG	PRO	817	26.554	-2.197	26.001	1.00	21.80
ATOM	1183	C	PRO	817	23.706	-4.320	26.458	1.00	22.95
ATOM	1184	O	PRO	817	22.988	-3.594	27.151	1.00	23.12
ATOM	1185	N	VAL	818	23.585	-5.640	26.418	1.00	24.79
ATOM	1186	CA	VAL	818	22.544	-6.316	27.195	1.00	26.35
ATOM	1187	CB	VAL	818	22.513	-7.860	26.916	1.00	27.19
ATOM	1188	CG1	VAL	818	23.864	-8.515	27.282	1.00	27.82
ATOM	1189	CG2	VAL	818	21.362	-8.524	27.676	1.00	27.72
ATOM	1190	C	VAL	818	22.742	-6.047	28.692	1.00	26.79
ATOM	1191	O	VAL	818	21.777	-5.849	29.421	1.00	26.79
ATOM	1192	N	ASP	819	23.992	-5.963	29.136	1.00	27.83
ATOM	1193	CA	ASP	819	24.240	-5.732	30.550	1.00	29.78
ATOM	1194	CB	ASP	819	25.406	-6.593	31.063	1.00	32.59
ATOM	1195	CG	ASP	819	26.747	-5.908	30.959	1.00	35.35
ATOM	1196	OD1	ASP	819	27.117	-5.518	29.825	1.00	38.62
ATOM	1197	OD2	ASP	819	27.431	-5.776	32.011	1.00	36.18
ATOM	1198	C	ASP	819	24.377	-4.266	30.937	1.00	29.73
ATOM	1199	O	ASP	819	24.899	-3.930	32.007	1.00	30.00
ATOM	1200	N	GLY	820	23.839	-3.403	30.085	1.00	29.43
ATOM	1201	CA	GLY	820	23.878	-1.974	30.342	1.00	28.69
ATOM	1202	C	GLY	820	25.216	-1.317	30.125	1.00	27.42
ATOM	1203	O	GLY	820	26.221	-1.982	29.938	1.00	26.73
ATOM	1204	N	LEU	821	25.208	0.010	30.135	1.00	28.29
ATOM	1205	CA	LEU	821	26.410	0.831	29.947	1.00	28.64
ATOM	1206	CB	LEU	821	26.023	2.110	29.195	1.00	28.29
ATOM	1207	CG	LEU	821	25.083	1.940	27.991	1.00	28.32
ATOM	1208	CD1	LEU	821	24.046	3.022	28.031	1.00	27.27
ATOM	1209	CD2	LEU	821	25.831	1.953	26.653	1.00	27.18
ATOM	1210	C	LEU	821	26.948	1.164	31.349	1.00	28.62
ATOM	1211	O	LEU	821	26.341	0.747	32.342	1.00	28.84
ATOM	1212	N	LYS	822	28.060	1.897	31.441	1.00	28.49
ATOM	1213	CA	LYS	822	28.642	2.268	32.741	1.00	29.80
ATOM	1214	CB	LYS	822	29.865	3.169	32.576	1.00	30.45
ATOM	1215	CG	LYS	822	30.924	2.626	31.666	1.00	32.84
ATOM	1216	CD	LYS	822	31.517	1.345	32.194	1.00	35.27
ATOM	1217	CE	LYS	822	32.433	0.688	31.161	1.00	36.20
ATOM	1218	NZ	LYS	822	33.498	1.623	30.710	1.00	37.22
ATOM	1219	C	LYS	822	27.621	3.016	33.587	1.00	30.25
ATOM	1220	O	LYS	822	27.353	2.655	34.731	1.00	31.02
ATOM	1221	N	ASN	823	27.065	4.080	33.029	1.00	29.98
ATOM	1222	CA	ASN	823	26.070	4.852	33.735	1.00	29.55
ATOM	1223	CB	ASN	823	26.458	6.323	33.774	1.00	31.17
ATOM	1224	CG	ASN	823	27.832	6.544	34.350	1.00	32.55
ATOM	1225	OD1	ASN	823	28.787	5.856	33.985	1.00	33.56
ATOM	1226	ND2	ASN	823	27.952	7.520	35.246	1.00	34.42
ATOM	1227	C	ASN	823	24.807	4.665	32.943	1.00	28.73
ATOM	1228	O	ASN	823	24.476	5.473	32.091	1.00	29.00
ATOM	1229	N	GLN	824	24.127	3.562	33.199	1.00	27.99
ATOM	1230	CA	GLN	824	22.893	3.227	32.514	1.00	27.77
ATOM	1231	CB	GLN	824	22.590	1.731	32.738	1.00	28.13
ATOM	1232	CG	GLN	824	21.343	1.158	32.077	1.00	28.93
ATOM	1233	CD	GLN	824	21.331	1.302	30.551	1.00	30.20
ATOM	1234	OE1	GLN	824	22.300	0.976	29.855	1.00	30.02
ATOM	1235	NE2	GLN	824	20.211	1.775	30.028	1.00	29.72
ATOM	1236	C	GLN	824	21.723	4.115	32.960	1.00	27.61

ATOM	1237	O	GLN	824	20.747	4.275	32.226	1.00	27.58
ATOM	1238	N	LYS	825	21.833	4.752	34.122	1.00	27.13
ATOM	1239	CA	LYS	825	20.742	5.590	34.595	1.00	26.37
ATOM	1240	CB	LYS	825	20.815	5.802	36.113	1.00	28.08
ATOM	1241	CG	LYS	825	19.430	5.823	36.792	1.00	31.02
ATOM	1242	CD	LYS	825	19.493	5.693	38.335	1.00	33.41
ATOM	1243	CE	LYS	825	18.086	5.725	39.002	1.00	34.57
ATOM	1244	NZ	LYS	825	17.196	4.516	38.739	1.00	35.55
ATOM	1245	C	LYS	825	20.679	6.917	33.876	1.00	24.74
ATOM	1246	O	LYS	825	19.625	7.518	33.799	1.00	25.30
ATOM	1247	N	PHE	826	21.794	7.375	33.330	1.00	24.06
ATOM	1248	CA	PHE	826	21.830	8.646	32.597	1.00	23.44
ATOM	1249	CB	PHE	826	23.247	9.191	32.573	1.00	25.61
ATOM	1250	CG	PHE	826	23.768	9.527	33.930	1.00	28.86
ATOM	1251	CD1	PHE	826	22.916	10.067	34.890	1.00	29.49
ATOM	1252	CD2	PHE	826	25.091	9.284	34.268	1.00	29.08
ATOM	1253	CE1	PHE	826	23.373	10.356	36.156	1.00	29.57
ATOM	1254	CE2	PHE	826	25.551	9.571	35.533	1.00	29.80
ATOM	1255	CZ	PHE	826	24.688	10.108	36.479	1.00	30.14
ATOM	1256	C	PHE	826	21.344	8.463	31.178	1.00	21.78
ATOM	1257	O	PHE	826	20.808	9.380	30.568	1.00	21.42
ATOM	1258	N	PHE	827	21.581	7.277	30.636	1.00	20.42
ATOM	1259	CA	PHE	827	21.145	6.937	29.299	1.00	18.74
ATOM	1260	CB	PHE	827	21.814	5.644	28.857	1.00	17.62
ATOM	1261	CG	PHE	827	21.238	5.083	27.610	1.00	16.77
ATOM	1262	CD1	PHE	827	21.780	5.412	26.380	1.00	16.74
ATOM	1263	CD2	PHE	827	20.123	4.261	27.656	1.00	16.46
ATOM	1264	CE1	PHE	827	21.225	4.939	25.212	1.00	16.50
ATOM	1265	CE2	PHE	827	19.555	3.782	26.491	1.00	17.41
ATOM	1266	CZ	PHE	827	20.105	4.120	25.266	1.00	16.35
ATOM	1267	C	PHE	827	19.627	6.778	29.277	1.00	19.19
ATOM	1268	O	PHE	827	18.962	7.183	28.331	1.00	18.79
ATOM	1269	N	ASP	828	19.079	6.150	30.312	1.00	20.42
ATOM	1270	CA	ASP	828	17.638	5.943	30.421	1.00	21.69
ATOM	1271	CB	ASP	828	17.325	5.045	31.633	1.00	23.37
ATOM	1272	CG	ASP	828	17.885	3.627	31.487	1.00	24.46
ATOM	1273	OD1	ASP	828	17.900	3.095	30.365	1.00	26.34
ATOM	1274	OD2	ASP	828	18.296	3.023	32.501	1.00	26.77
ATOM	1275	C	ASP	828	16.931	7.287	30.572	1.00	21.41
ATOM	1276	O	ASP	828	15.835	7.487	30.070	1.00	21.87
ATOM	1277	N	GLU	829	17.552	8.187	31.313	1.00	22.11
ATOM	1278	CA	GLU	829	17.005	9.510	31.533	1.00	23.92
ATOM	1279	CB	GLU	829	17.910	10.309	32.499	1.00	27.77
ATOM	1280	CG	GLU	829	18.168	11.823	32.130	1.00	32.20
ATOM	1281	CD	GLU	829	19.650	12.266	32.334	1.00	35.29
ATOM	1282	OE1	GLU	829	20.005	12.655	33.482	1.00	37.06
ATOM	1283	OE2	GLU	829	20.463	12.217	31.360	1.00	34.89
ATOM	1284	C	GLU	829	17.011	10.166	30.174	1.00	22.78
ATOM	1285	O	GLU	829	15.963	10.539	29.656	1.00	22.06
ATOM	1286	N	LEU	830	18.201	10.200	29.575	1.00	22.21
ATOM	1287	CA	LEU	830	18.437	10.812	28.272	1.00	22.14
ATOM	1288	CB	LEU	830	19.885	10.575	27.852	1.00	21.24
ATOM	1289	CG	LEU	830	20.415	11.572	26.833	1.00	21.76
ATOM	1290	CD1	LEU	830	20.037	13.004	27.215	1.00	21.40
ATOM	1291	CD2	LEU	830	21.895	11.429	26.752	1.00	22.34
ATOM	1292	C	LEU	830	17.499	10.318	27.191	1.00	22.74
ATOM	1293	O	LEU	830	16.874	11.114	26.481	1.00	23.35
ATOM	1294	N	ARG	831	17.400	9.002	27.079	1.00	22.23
ATOM	1295	CA	ARG	831	16.559	8.352	26.097	1.00	22.37
ATOM	1296	CB	ARG	831	16.780	6.849	26.186	1.00	22.50
ATOM	1297	CG	ARG	831	15.957	6.087	25.219	1.00	22.59
ATOM	1298	CD	ARG	831	16.130	4.600	25.375	1.00	23.29

ATOM	1299	NE	ARG	831	15.921	3.972	24.074	1.00	25.50
ATOM	1300	CZ	ARG	831	14.738	3.800	23.491	1.00	24.36
ATOM	1301	NH1	ARG	831	13.632	4.173	24.096	1.00	25.37
ATOM	1302	NH2	ARG	831	14.676	3.366	22.250	1.00	24.31
ATOM	1303	C	ARG	831	15.086	8.667	26.302	1.00	22.46
ATOM	1304	O	ARG	831	14.354	8.964	25.351	1.00	22.89
ATOM	1305	N	MET	832	14.655	8.593	27.550	1.00	22.76
ATOM	1306	CA	MET	832	13.276	8.859	27.923	1.00	22.91
ATOM	1307	CB	MET	832	13.126	8.762	29.429	1.00	23.88
ATOM	1308	CG	MET	832	11.739	9.050	29.870	1.00	24.65
ATOM	1309	SD	MET	832	11.693	9.332	31.596	1.00	29.43
ATOM	1310	CE	MET	832	10.059	10.026	31.651	1.00	29.67
ATOM	1311	C	MET	832	12.879	10.262	27.513	1.00	23.47
ATOM	1312	O	MET	832	11.740	10.512	27.097	1.00	23.79
ATOM	1313	N	ASN	833	13.782	11.198	27.768	1.00	23.63
ATOM	1314	CA	ASN	833	13.562	12.599	27.423	1.00	23.80
ATOM	1315	CB	ASN	833	14.676	13.482	28.013	1.00	23.64
ATOM	1316	CG	ASN	833	14.532	13.679	29.544	1.00	23.87
ATOM	1317	OD1	ASN	833	15.519	13.864	30.270	1.00	23.24
ATOM	1318	ND2	ASN	833	13.293	13.628	30.030	1.00	24.57
ATOM	1319	C	ASN	833	13.403	12.761	25.905	1.00	23.94
ATOM	1320	O	ASN	833	12.463	13.397	25.445	1.00	24.48
ATOM	1321	N	TYR	834	14.240	12.093	25.123	1.00	23.69
ATOM	1322	CA	TYR	834	14.121	12.165	23.673	1.00	24.70
ATOM	1323	CB	TYR	834	15.340	11.532	23.007	1.00	25.39
ATOM	1324	CG	TYR	834	16.491	12.489	22.872	1.00	25.49
ATOM	1325	CD1	TYR	834	16.802	13.051	21.635	1.00	26.75
ATOM	1326	CE1	TYR	834	17.828	13.975	21.502	1.00	27.67
ATOM	1327	CD2	TYR	834	17.239	12.869	23.986	1.00	26.00
ATOM	1328	CE2	TYR	834	18.268	13.791	23.873	1.00	26.69
ATOM	1329	CZ	TYR	834	18.558	14.341	22.624	1.00	28.15
ATOM	1330	OH	TYR	834	19.571	15.263	22.497	1.00	28.86
ATOM	1331	C	TYR	834	12.809	11.574	23.128	1.00	24.43
ATOM	1332	O	TYR	834	12.297	12.006	22.082	1.00	24.26
ATOM	1333	N	ILE	835	12.260	10.599	23.843	1.00	24.33
ATOM	1334	CA	ILE	835	11.004	9.991	23.450	1.00	23.48
ATOM	1335	CB	ILE	835	10.724	8.727	24.235	1.00	21.33
ATOM	1336	CG2	ILE	835	9.297	8.308	24.054	1.00	19.87
ATOM	1337	CG1	ILE	835	11.657	7.624	23.756	1.00	20.40
ATOM	1338	CD1	ILE	835	11.684	6.400	24.655	1.00	21.05
ATOM	1339	C	ILE	835	9.893	10.977	23.687	1.00	25.05
ATOM	1340	O	ILE	835	8.972	11.061	22.889	1.00	26.24
ATOM	1341	N	LYS	836	9.998	11.738	24.771	1.00	26.82
ATOM	1342	CA	LYS	836	9.006	12.747	25.137	1.00	28.28
ATOM	1343	CB	LYS	836	9.245	13.281	26.556	1.00	29.95
ATOM	1344	CG	LYS	836	9.115	12.252	27.712	1.00	32.62
ATOM	1345	CD	LYS	836	7.690	11.672	27.901	1.00	33.04
ATOM	1346	CE	LYS	836	7.575	10.238	27.344	1.00	34.32
ATOM	1347	NZ	LYS	836	8.559	9.259	27.942	1.00	32.90
ATOM	1348	C	LYS	836	9.030	13.919	24.164	1.00	28.39
ATOM	1349	O	LYS	836	7.997	14.545	23.946	1.00	29.09
ATOM	1350	N	GLU	837	10.194	14.249	23.606	1.00	28.61
ATOM	1351	CA	GLU	837	10.276	15.351	22.643	1.00	28.70
ATOM	1352	CB	GLU	837	11.715	15.824	22.439	1.00	29.34
ATOM	1353	CG	GLU	837	12.305	16.584	23.627	1.00	32.13
ATOM	1354	CD	GLU	837	11.553	17.887	23.971	1.00	34.30
ATOM	1355	OE1	GLU	837	11.612	18.303	25.157	1.00	34.18
ATOM	1356	OE2	GLU	837	10.925	18.503	23.063	1.00	35.58
ATOM	1357	C	GLU	837	9.666	14.907	21.321	1.00	28.92
ATOM	1358	O	GLU	837	9.041	15.699	20.626	1.00	28.40
ATOM	1359	N	LEU	838	9.826	13.631	20.991	1.00	29.32
ATOM	1360	CA	LEU	838	9.250	13.092	19.774	1.00	30.90

ATOM	1361	CB	LEU	838	9.614	11.622	19.592	1.00	30.44
ATOM	1362	CG	LEU	838	8.810	10.983	18.460	1.00	30.56
ATOM	1363	CD1	LEU	838	9.077	11.728	17.151	1.00	30.31
ATOM	1364	CD2	LEU	838	9.166	9.533	18.330	1.00	30.00
ATOM	1365	C	LEU	838	7.740	13.211	19.884	1.00	32.66
ATOM	1366	O	LEU	838	7.076	13.706	18.983	1.00	32.60
ATOM	1367	N	ASP	839	7.186	12.724	20.979	1.00	34.82
ATOM	1368	CA	ASP	839	5.755	12.823	21.162	1.00	37.61
ATOM	1369	CB	ASP	839	5.331	12.117	22.449	1.00	39.22
ATOM	1370	CG	ASP	839	3.816	11.952	22.557	1.00	41.54
ATOM	1371	OD1	ASP	839	3.249	12.375	23.592	1.00	43.10
ATOM	1372	OD2	ASP	839	3.192	11.400	21.613	1.00	42.60
ATOM	1373	C	ASP	839	5.338	14.293	21.187	1.00	38.83
ATOM	1374	O	ASP	839	4.285	14.645	20.672	1.00	39.02
ATOM	1375	N	ARG	840	6.195	15.151	21.731	1.00	40.51
ATOM	1376	CA	ARG	840	5.916	16.580	21.828	1.00	42.20
ATOM	1377	CB	ARG	840	7.032	17.289	22.610	1.00	43.32
ATOM	1378	CG	ARG	840	6.657	18.639	23.261	1.00	45.47
ATOM	1379	CD	ARG	840	6.945	19.881	22.401	1.00	46.95
ATOM	1380	NE	ARG	840	8.319	20.371	22.542	1.00	48.57
ATOM	1381	CZ	ARG	840	9.066	20.823	21.533	1.00	49.57
ATOM	1382	NH1	ARG	840	8.580	20.860	20.294	1.00	49.89
ATOM	1383	NH2	ARG	840	10.314	21.220	21.755	1.00	49.90
ATOM	1384	C	ARG	840	5.776	17.220	20.457	1.00	43.27
ATOM	1385	O	ARG	840	4.860	18.004	20.232	1.00	43.50
ATOM	1386	N	ILE	841	6.663	16.876	19.528	1.00	44.53
ATOM	1387	CA	ILE	841	6.600	17.483	18.211	1.00	46.22
ATOM	1388	CB	ILE	841	7.983	17.572	17.510	1.00	45.82
ATOM	1389	CG2	ILE	841	9.044	18.078	18.463	1.00	46.40
ATOM	1390	CG1	ILE	841	8.383	16.237	16.918	1.00	46.46
ATOM	1391	CD1	ILE	841	8.064	16.150	15.463	1.00	45.92
ATOM	1392	C	ILE	841	5.534	16.913	17.286	1.00	48.04
ATOM	1393	O	ILE	841	5.472	17.272	16.109	1.00	48.90
ATOM	1394	N	ILE	842	4.737	15.976	17.786	1.00	49.91
ATOM	1395	CA	ILE	842	3.632	15.446	16.990	1.00	51.38
ATOM	1396	CB	ILE	842	3.577	13.878	16.889	1.00	51.11
ATOM	1397	CG2	ILE	842	3.917	13.445	15.482	1.00	51.75
ATOM	1398	CG1	ILE	842	4.523	13.192	17.870	1.00	50.67
ATOM	1399	CD1	ILE	842	4.691	11.701	17.619	1.00	49.36
ATOM	1400	C	ILE	842	2.384	16.003	17.659	1.00	52.63
ATOM	1401	O	ILE	842	1.509	16.551	16.999	1.00	52.38
ATOM	1402	N	ALA	843	2.356	15.939	18.986	1.00	54.81
ATOM	1403	CA	ALA	843	1.242	16.456	19.761	1.00	57.24
ATOM	1404	CB	ALA	843	1.424	16.129	21.247	1.00	56.69
ATOM	1405	C	ALA	843	1.215	17.962	19.557	1.00	59.28
ATOM	1406	O	ALA	843	1.847	18.704	20.304	1.00	59.69
ATOM	1407	N	CYS	844	0.560	18.391	18.481	1.00	61.60
ATOM	1408	CA	CYS	844	0.402	19.810	18.130	1.00	63.67
ATOM	1409	CB	CYS	844	1.766	20.536	17.979	1.00	64.05
ATOM	1410	SG	CYS	844	2.751	20.268	16.470	1.00	65.30
ATOM	1411	C	CYS	844	-0.441	19.854	16.848	1.00	64.63
ATOM	1412	O	CYS	844	-1.618	19.471	16.889	1.00	64.70
ATOM	1413	N	ALA	845	0.136	20.332	15.738	1.00	65.65
ATOM	1414	CA	ALA	845	-0.545	20.374	14.439	1.00	65.96
ATOM	1415	CB	ALA	845	-0.195	21.639	13.684	1.00	65.80
ATOM	1416	C	ALA	845	-0.079	19.165	13.644	1.00	66.49
ATOM	1417	O	ALA	845	-0.675	18.829	12.620	1.00	66.85
ATOM	1418	N	ALA	846	0.998	18.533	14.127	1.00	66.74
ATOM	1419	CA	ALA	846	1.601	17.343	13.511	1.00	66.90
ATOM	1420	CB	ALA	846	3.110	17.337	13.730	1.00	66.74
ATOM	1421	C	ALA	846	0.984	16.074	14.086	1.00	66.88
ATOM	1422	O	ALA	846	1.675	15.092	14.345	1.00	66.35

ATOM	1423	N	ALA	847	-0.325	16.141	14.291	1.00	67.27
ATOM	1424	CA	ALA	847	-1.162	15.076	14.826	1.00	67.87
ATOM	1425	CB	ALA	847	-0.515	14.407	16.033	1.00	68.14
ATOM	1426	C	ALA	847	-2.420	15.816	15.251	1.00	68.35
ATOM	1427	O	ALA	847	-2.432	17.046	15.278	1.00	68.33
ATOM	1428	N	ALA	848	-3.468	15.079	15.597	1.00	69.11
ATOM	1429	CA	ALA	848	-4.728	15.685	16.016	1.00	69.71
ATOM	1430	CB	ALA	848	-5.272	16.598	14.907	1.00	69.68
ATOM	1431	C	ALA	848	-5.737	14.586	16.340	1.00	70.20
ATOM	1432	O	ALA	848	-5.342	13.474	16.720	1.00	70.21
ATOM	1433	N	ALA	849	-7.021	14.914	16.146	1.00	70.54
ATOM	1434	CA	ALA	849	-8.185	14.043	16.374	1.00	70.31
ATOM	1435	CB	ALA	849	-9.014	13.929	15.079	1.00	70.65
ATOM	1436	C	ALA	849	-7.856	12.661	16.920	1.00	69.92
ATOM	1437	O	ALA	849	-7.665	12.492	18.130	1.00	70.12
ATOM	1438	N	ALA	850	-7.808	11.680	16.020	1.00	69.47
ATOM	1439	CA	ALA	850	-7.473	10.304	16.377	1.00	68.74
ATOM	1440	CB	ALA	850	-8.494	9.331	15.774	1.00	68.95
ATOM	1441	C	ALA	850	-6.061	10.015	15.845	1.00	67.76
ATOM	1442	O	ALA	850	-5.590	8.867	15.864	1.00	67.27
ATOM	1443	N	SER	851	-5.391	11.077	15.388	1.00	66.46
ATOM	1444	CA	SER	851	-4.046	10.962	14.846	1.00	65.28
ATOM	1445	CB	SER	851	-3.664	12.200	14.018	1.00	65.24
ATOM	1446	OG	SER	851	-2.405	12.037	13.369	1.00	65.05
ATOM	1447	C	SER	851	-3.023	10.710	15.944	1.00	64.16
ATOM	1448	O	SER	851	-2.426	9.639	15.969	1.00	64.16
ATOM	1449	N	CYS	852	-2.873	11.651	16.879	1.00	62.68
ATOM	1450	CA	CYS	852	-1.901	11.526	17.974	1.00	60.96
ATOM	1451	CB	CYS	852	-2.353	12.333	19.191	1.00	61.34
ATOM	1452	SG	CYS	852	-1.712	14.024	19.216	1.00	62.06
ATOM	1453	C	CYS	852	-1.480	10.102	18.388	1.00	59.71
ATOM	1454	O	CYS	852	-0.282	9.800	18.422	1.00	59.67
ATOM	1455	N	SER	853	-2.440	9.223	18.678	1.00	57.85
ATOM	1456	CA	SER	853	-2.109	7.847	19.053	1.00	55.45
ATOM	1457	CB	SER	853	-3.308	7.133	19.686	1.00	56.27
ATOM	1458	OG	SER	853	-3.480	7.522	21.038	1.00	57.65
ATOM	1459	C	SER	853	-1.610	7.052	17.847	1.00	53.09
ATOM	1460	O	SER	853	-0.601	6.346	17.942	1.00	53.22
ATOM	1461	N	ARG	854	-2.304	7.172	16.719	1.00	49.75
ATOM	1462	CA	ARG	854	-1.924	6.462	15.500	1.00	46.39
ATOM	1463	CB	ARG	854	-3.021	6.634	14.443	1.00	47.23
ATOM	1464	CG	ARG	854	-2.747	5.970	13.105	1.00	48.09
ATOM	1465	CD	ARG	854	-2.985	6.943	11.940	1.00	49.85
ATOM	1466	NE	ARG	854	-4.340	7.500	11.936	1.00	51.11
ATOM	1467	CZ	ARG	854	-4.911	8.122	10.904	1.00	51.20
ATOM	1468	NH1	ARG	854	-4.261	8.290	9.755	1.00	51.32
ATOM	1469	NH2	ARG	854	-6.153	8.567	11.021	1.00	51.21
ATOM	1470	C	ARG	854	-0.564	6.962	14.967	1.00	43.72
ATOM	1471	O	ARG	854	0.294	6.164	14.564	1.00	43.80
ATOM	1472	N	ARG	855	-0.360	8.273	15.019	1.00	39.68
ATOM	1473	CA	ARG	855	0.860	8.926	14.558	1.00	36.58
ATOM	1474	CB	ARG	855	0.713	10.439	14.734	1.00	36.42
ATOM	1475	CG	ARG	855	1.801	11.264	14.082	1.00	34.79
ATOM	1476	CD	ARG	855	1.724	11.109	12.594	1.00	32.86
ATOM	1477	NE	ARG	855	2.869	11.699	11.907	1.00	30.54
ATOM	1478	CZ	ARG	855	3.030	11.655	10.590	1.00	29.61
ATOM	1479	NH1	ARG	855	2.130	11.051	9.831	1.00	28.88
ATOM	1480	NH2	ARG	855	4.085	12.219	10.028	1.00	29.20
ATOM	1481	C	ARG	855	2.106	8.454	15.306	1.00	35.02
ATOM	1482	O	ARG	855	3.180	8.326	14.723	1.00	34.97
ATOM	1483	N	PHE	856	1.973	8.239	16.609	1.00	33.30
ATOM	1484	CA	PHE	856	3.086	7.786	17.428	1.00	31.21

ATOM	1485	CB	PHE	856	2.846	8.128	18.895	1.00	30.24
ATOM	1486	CG	PHE	856	4.058	7.977	19.755	1.00	30.06
ATOM	1487	CD1	PHE	856	5.022	8.972	19.787	1.00	29.34
ATOM	1488	CD2	PHE	856	4.241	6.829	20.536	1.00	29.33
ATOM	1489	CE1	PHE	856	6.150	8.832	20.580	1.00	29.36
ATOM	1490	CE2	PHE	856	5.364	6.676	21.335	1.00	28.86
ATOM	1491	CZ	PHE	856	6.325	7.680	21.357	1.00	29.62
ATOM	1492	C	PHE	856	3.308	6.290	17.254	1.00	30.61
ATOM	1493	O	PHE	856	4.420	5.803	17.424	1.00	30.75
ATOM	1494	N	TYR	857	2.258	5.543	16.943	1.00	29.79
ATOM	1495	CA	TYR	857	2.446	4.118	16.725	1.00	29.79
ATOM	1496	CB	TYR	857	1.116	3.365	16.660	1.00	30.78
ATOM	1497	CG	TYR	857	1.254	1.871	16.396	1.00	32.21
ATOM	1498	CD1	TYR	857	1.425	0.972	17.442	1.00	32.75
ATOM	1499	CE1	TYR	857	1.548	-0.401	17.215	1.00	34.60
ATOM	1500	CD2	TYR	857	1.208	1.362	15.098	1.00	33.36
ATOM	1501	CE2	TYR	857	1.331	-0.011	14.854	1.00	34.67
ATOM	1502	CZ	TYR	857	1.503	-0.887	15.918	1.00	35.61
ATOM	1503	OH	TYR	857	1.652	-2.244	15.697	1.00	36.96
ATOM	1504	C	TYR	857	3.206	3.929	15.419	1.00	29.44
ATOM	1505	O	TYR	857	4.135	3.125	15.371	1.00	29.44
ATOM	1506	N	GLN	858	2.847	4.685	14.376	1.00	28.32
ATOM	1507	CA	GLN	858	3.533	4.537	13.087	1.00	28.06
ATOM	1508	CB	GLN	858	2.675	5.020	11.890	1.00	28.98
ATOM	1509	CG	GLN	858	1.970	6.384	12.029	1.00	31.65
ATOM	1510	CD	GLN	858	0.781	6.569	11.059	1.00	32.26
ATOM	1511	OE1	GLN	858	0.385	7.700	10.724	1.00	32.11
ATOM	1512	NE2	GLN	858	0.210	5.458	10.617	1.00	32.79
ATOM	1513	C	GLN	858	4.967	5.077	13.037	1.00	26.56
ATOM	1514	O	GLN	858	5.820	4.525	12.332	1.00	26.58
ATOM	1515	N	LEU	859	5.266	6.101	13.825	1.00	24.64
ATOM	1516	CA	LEU	859	6.622	6.632	13.832	1.00	22.82
ATOM	1517	CB	LEU	859	6.675	8.067	14.395	1.00	23.93
ATOM	1518	CG	LEU	859	6.054	9.243	13.617	1.00	23.18
ATOM	1519	CD1	LEU	859	6.616	10.541	14.156	1.00	23.42
ATOM	1520	CD2	LEU	859	6.363	9.137	12.173	1.00	22.30
ATOM	1521	C	LEU	859	7.545	5.705	14.613	1.00	20.92
ATOM	1522	O	LEU	859	8.694	5.486	14.222	1.00	20.35
ATOM	1523	N	THR	860	7.030	5.124	15.691	1.00	20.30
ATOM	1524	CA	THR	860	7.821	4.195	16.505	1.00	20.14
ATOM	1525	CB	THR	860	7.215	3.957	17.905	1.00	18.65
ATOM	1526	OG1	THR	860	5.849	3.551	17.797	1.00	18.55
ATOM	1527	CG2	THR	860	7.314	5.196	18.734	1.00	18.12
ATOM	1528	C	THR	860	7.969	2.855	15.765	1.00	20.30
ATOM	1529	O	THR	860	8.922	2.108	15.985	1.00	20.28
ATOM	1530	N	LYS	861	7.040	2.600	14.851	1.00	21.02
ATOM	1531	CA	LYS	861	7.046	1.411	14.034	1.00	21.82
ATOM	1532	CB	LYS	861	5.649	1.178	13.475	1.00	23.82
ATOM	1533	CG	LYS	861	5.375	-0.268	13.110	1.00	26.71
ATOM	1534	CD	LYS	861	5.015	-1.106	14.321	1.00	28.40
ATOM	1535	CE	LYS	861	4.924	-2.587	13.922	1.00	30.14
ATOM	1536	NZ	LYS	861	4.542	-3.514	15.050	1.00	31.53
ATOM	1537	C	LYS	861	8.040	1.642	12.895	1.00	21.28
ATOM	1538	O	LYS	861	8.781	0.750	12.510	1.00	21.01
ATOM	1539	N	LEU	862	8.093	2.863	12.389	1.00	21.49
ATOM	1540	CA	LEU	862	9.021	3.192	11.311	1.00	21.32
ATOM	1541	CB	LEU	862	8.713	4.577	10.731	1.00	22.14
ATOM	1542	CG	LEU	862	9.816	5.281	9.921	1.00	21.98
ATOM	1543	CD1	LEU	862	10.022	4.563	8.622	1.00	22.72
ATOM	1544	CD2	LEU	862	9.456	6.726	9.670	1.00	22.58
ATOM	1545	C	LEU	862	10.438	3.181	11.854	1.00	21.15
ATOM	1546	O	LEU	862	11.386	2.884	11.133	1.00	22.30

ATOM	1547	N	LEU	863	10.596	3.602	13.105	1.00	20.71
ATOM	1548	CA	LEU	863	11.906	3.625	13.749	1.00	18.90
ATOM	1549	CB	LEU	863	11.827	4.423	15.040	1.00	18.78
ATOM	1550	CG	LEU	863	11.890	5.931	14.863	1.00	18.02
ATOM	1551	CD1	LEU	863	12.103	6.545	16.230	1.00	19.67
ATOM	1552	CD2	LEU	863	13.049	6.291	13.944	1.00	16.59
ATOM	1553	C	LEU	863	12.462	2.218	14.004	1.00	18.08
ATOM	1554	O	LEU	863	13.676	1.984	13.895	1.00	17.06
ATOM	1555	N	ASP	864	11.592	1.307	14.436	1.00	18.33
ATOM	1556	CA	ASP	864	11.985	-0.088	14.642	1.00	19.28
ATOM	1557	CB	ASP	864	10.797	-0.917	15.143	1.00	19.27
ATOM	1558	CG	ASP	864	10.525	-0.727	16.620	1.00	19.92
ATOM	1559	OD1	ASP	864	11.256	0.045	17.271	1.00	20.94
ATOM	1560	OD2	ASP	864	9.577	-1.364	17.116	1.00	19.39
ATOM	1561	C	ASP	864	12.467	-0.692	13.321	1.00	19.06
ATOM	1562	O	ASP	864	13.377	-1.519	13.298	1.00	18.82
ATOM	1563	N	SER	865	11.847	-0.263	12.222	1.00	19.90
ATOM	1564	CA	SER	865	12.202	-0.764	10.894	1.00	19.17
ATOM	1565	CB	SER	865	11.226	-0.289	9.798	1.00	18.59
ATOM	1566	OG	SER	865	11.167	1.123	9.613	1.00	19.91
ATOM	1567	C	SER	865	13.634	-0.507	10.489	1.00	18.01
ATOM	1568	O	SER	865	14.213	-1.294	9.765	1.00	18.93
ATOM	1569	N	VAL	866	14.257	0.535	11.004	1.00	17.08
ATOM	1570	CA	VAL	866	15.619	0.747	10.589	1.00	15.20
ATOM	1571	CB	VAL	866	16.093	2.211	10.783	1.00	15.01
ATOM	1572	CG1	VAL	866	14.982	3.081	11.320	1.00	13.81
ATOM	1573	CG2	VAL	866	17.344	2.280	11.574	1.00	13.41
ATOM	1574	C	VAL	866	16.564	-0.260	11.194	1.00	14.83
ATOM	1575	O	VAL	866	17.625	-0.518	10.641	1.00	14.66
ATOM	1576	N	GLN	867	16.168	-0.873	12.302	1.00	15.12
ATOM	1577	CA	GLN	867	17.031	-1.849	12.977	1.00	15.64
ATOM	1578	CB	GLN	867	16.508	-2.155	14.374	1.00	16.10
ATOM	1579	CG	GLN	867	16.526	-0.968	15.315	1.00	16.35
ATOM	1580	CD	GLN	867	17.910	-0.474	15.672	1.00	17.91
ATOM	1581	OE1	GLN	867	18.924	-1.175	15.510	1.00	17.76
ATOM	1582	NE2	GLN	867	17.958	0.750	16.201	1.00	17.53
ATOM	1583	C	GLN	867	17.358	-3.143	12.233	1.00	14.54
ATOM	1584	O	GLN	867	18.487	-3.594	12.271	1.00	15.92
ATOM	1585	N	PRO	868	16.364	-3.809	11.634	1.00	14.35
ATOM	1586	CD	PRO	868	14.914	-3.555	11.696	1.00	15.17
ATOM	1587	CA	PRO	868	16.630	-5.040	10.886	1.00	13.73
ATOM	1588	CB	PRO	868	15.232	-5.465	10.415	1.00	14.35
ATOM	1589	CG	PRO	868	14.331	-4.928	11.438	1.00	14.42
ATOM	1590	C	PRO	868	17.500	-4.704	9.674	1.00	13.45
ATOM	1591	O	PRO	868	18.341	-5.497	9.254	1.00	14.77
ATOM	1592	N	ILE	869	17.289	-3.514	9.113	1.00	13.49
ATOM	1593	CA	ILE	869	18.043	-3.044	7.970	1.00	12.06
ATOM	1594	CB	ILE	869	17.447	-1.740	7.358	1.00	12.53
ATOM	1595	CG2	ILE	869	18.272	-1.307	6.175	1.00	12.44
ATOM	1596	CG1	ILE	869	15.998	-1.973	6.928	1.00	12.25
ATOM	1597	CD1	ILE	869	15.258	-0.746	6.432	1.00	11.91
ATOM	1598	C	ILE	869	19.458	-2.818	8.411	1.00	11.70
ATOM	1599	O	ILE	869	20.356	-3.302	7.755	1.00	13.01
ATOM	1600	N	ALA	870	19.655	-2.254	9.610	1.00	12.19
ATOM	1601	CA	ALA	870	21.007	-1.993	10.110	1.00	11.52
ATOM	1602	CB	ALA	870	20.971	-1.189	11.375	1.00	10.62
ATOM	1603	C	ALA	870	21.758	-3.287	10.350	1.00	12.90
ATOM	1604	O	ALA	870	22.955	-3.374	10.074	1.00	13.99
ATOM	1605	N	ARG	871	21.082	-4.262	10.962	1.00	14.67
ATOM	1606	CA	ARG	871	21.659	-5.577	11.226	1.00	15.30
ATOM	1607	CB	ARG	871	20.668	-6.465	11.970	1.00	16.99
ATOM	1608	CG	ARG	871	21.317	-7.789	12.304	1.00	20.44

ATOM	1609	CD	ARG	871	20.552	-8.755	13.190	1.00	22.19
ATOM	1610	NE	ARG	871	21.529	-9.736	13.678	1.00	25.05
ATOM	1611	CZ	ARG	871	22.248	-9.581	14.785	1.00	24.87
ATOM	1612	NH1	ARG	871	22.085	-8.513	15.553	1.00	26.86
ATOM	1613	NH2	ARG	871	23.221	-10.425	15.059	1.00	27.12
ATOM	1614	C	ARG	871	22.119	-6.287	9.939	1.00	16.18
ATOM	1615	O	ARG	871	23.216	-6.846	9.897	1.00	16.90
ATOM	1616	N	GLU	872	21.300	-6.256	8.886	1.00	17.08
ATOM	1617	CA	GLU	872	21.669	-6.874	7.595	1.00	17.70
ATOM	1618	CB	GLU	872	20.546	-6.670	6.578	1.00	20.21
ATOM	1619	CG	GLU	872	20.070	-7.920	5.827	1.00	27.32
ATOM	1620	CD	GLU	872	19.041	-7.600	4.715	1.00	31.24
ATOM	1621	OE1	GLU	872	19.199	-8.069	3.544	1.00	32.65
ATOM	1622	OE2	GLU	872	18.068	-6.867	5.018	1.00	33.14
ATOM	1623	C	GLU	872	22.961	-6.229	7.064	1.00	16.22
ATOM	1624	O	GLU	872	23.826	-6.892	6.504	1.00	16.64
ATOM	1625	N	LEU	873	23.109	-4.927	7.254	1.00	15.48
ATOM	1626	CA	LEU	873	24.304	-4.230	6.781	1.00	13.64
ATOM	1627	CB	LEU	873	24.040	-2.718	6.664	1.00	13.09
ATOM	1628	CG	LEU	873	22.957	-2.359	5.640	1.00	12.60
ATOM	1629	CD1	LEU	873	22.396	-0.985	5.856	1.00	13.12
ATOM	1630	CD2	LEU	873	23.511	-2.529	4.229	1.00	12.29
ATOM	1631	C	LEU	873	25.489	-4.510	7.662	1.00	13.26
ATOM	1632	O	LEU	873	26.621	-4.541	7.185	1.00	12.91
ATOM	1633	N	HIS	874	25.237	-4.688	8.960	1.00	14.96
ATOM	1634	CA	HIS	874	26.297	-5.011	9.935	1.00	15.73
ATOM	1635	CB	HIS	874	25.735	-5.154	11.351	1.00	14.09
ATOM	1636	CG	HIS	874	25.513	-3.860	12.062	1.00	13.53
ATOM	1637	CD2	HIS	874	26.303	-2.769	12.204	1.00	12.74
ATOM	1638	ND1	HIS	874	24.365	-3.588	12.771	1.00	12.74
ATOM	1639	CE1	HIS	874	24.451	-2.397	13.313	1.00	11.45
ATOM	1640	NE2	HIS	874	25.616	-1.878	12.990	1.00	10.87
ATOM	1641	C	HIS	874	26.945	-6.342	9.549	1.00	16.66
ATOM	1642	O	HIS	874	28.171	-6.454	9.539	1.00	16.68
ATOM	1643	N	GLN	875	26.122	-7.356	9.268	1.00	18.67
ATOM	1644	CA	GLN	875	26.635	-8.674	8.853	1.00	19.45
ATOM	1645	CB	GLN	875	25.507	-9.726	8.779	1.00	21.56
ATOM	1646	CG	GLN	875	25.566	-10.875	9.864	1.00	25.76
ATOM	1647	CD	GLN	875	26.681	-11.938	9.671	1.00	26.74
ATOM	1648	OE1	GLN	875	27.871	-11.624	9.654	1.00	27.36
ATOM	1649	NE2	GLN	875	26.285	-13.204	9.589	1.00	27.93
ATOM	1650	C	GLN	875	27.324	-8.521	7.491	1.00	18.37
ATOM	1651	O	GLN	875	28.428	-9.022	7.294	1.00	18.65
ATOM	1652	N	PHE	876	26.737	-7.724	6.597	1.00	18.47
ATOM	1653	CA	PHE	876	27.338	-7.515	5.280	1.00	18.22
ATOM	1654	CB	PHE	876	26.453	-6.641	4.377	1.00	19.25
ATOM	1655	CG	PHE	876	26.966	-6.506	2.954	1.00	19.63
ATOM	1656	CD1	PHE	876	28.038	-5.675	2.657	1.00	18.97
ATOM	1657	CD2	PHE	876	26.380	-7.226	1.917	1.00	19.90
ATOM	1658	CE1	PHE	876	28.519	-5.558	1.343	1.00	20.30
ATOM	1659	CE2	PHE	876	26.857	-7.113	0.597	1.00	20.70
ATOM	1660	CZ	PHE	876	27.926	-6.281	0.310	1.00	18.82
ATOM	1661	C	PHE	876	28.689	-6.871	5.403	1.00	17.76
ATOM	1662	O	PHE	876	29.687	-7.412	4.920	1.00	17.95
ATOM	1663	N	THR	877	28.741	-5.732	6.086	1.00	17.85
ATOM	1664	CA	THR	877	30.002	-5.024	6.215	1.00	17.77
ATOM	1665	CB	THR	877	29.855	-3.641	6.915	1.00	18.24
ATOM	1666	OG1	THR	877	30.954	-2.808	6.525	1.00	19.13
ATOM	1667	CG2	THR	877	29.868	-3.765	8.444	1.00	17.92
ATOM	1668	C	THR	877	31.040	-5.884	6.900	1.00	17.52
ATOM	1669	O	THR	877	32.208	-5.849	6.514	1.00	16.51
ATOM	1670	N	PHE	878	30.634	-6.610	7.943	1.00	18.06

ATOM	1671	CA	PHE	878	31.559	-7.501	8.651	1.00	19.20
ATOM	1672	CB	PHE	878	30.863	-8.201	9.805	1.00	19.53
ATOM	1673	CG	PHE	878	31.731	-9.220	10.484	1.00	20.60
ATOM	1674	CD1	PHE	878	32.681	-8.829	11.414	1.00	19.88
ATOM	1675	CD2	PHE	878	31.623	-10.575	10.150	1.00	20.59
ATOM	1676	CE1	PHE	878	33.518	-9.774	12.008	1.00	22.10
ATOM	1677	CE2	PHE	878	32.454	-11.532	10.733	1.00	20.21
ATOM	1678	CZ	PHE	878	33.403	-11.138	11.660	1.00	20.82
ATOM	1679	C	PHE	878	32.176	-8.567	7.725	1.00	18.91
ATOM	1680	O	PHE	878	33.400	-8.724	7.670	1.00	17.63
ATOM	1681	N	ASP	879	31.326	-9.268	6.973	1.00	19.57
ATOM	1682	CA	ASP	879	31.800	-10.301	6.054	1.00	20.02
ATOM	1683	CB	ASP	879	30.622	-10.972	5.342	1.00	20.24
ATOM	1684	CG	ASP	879	29.693	-11.724	6.307	1.00	22.04
ATOM	1685	OD1	ASP	879	30.122	-12.072	7.443	1.00	23.16
ATOM	1686	OD2	ASP	879	28.520	-11.968	5.937	1.00	21.98
ATOM	1687	C	ASP	879	32.723	-9.654	5.044	1.00	20.35
ATOM	1688	O	ASP	879	33.802	-10.171	4.737	1.00	20.51
ATOM	1689	N	LEU	880	32.342	-8.472	4.580	1.00	20.77
ATOM	1690	CA	LEU	880	33.149	-7.775	3.596	1.00	20.33
ATOM	1691	CB	LEU	880	32.484	-6.471	3.180	1.00	20.23
ATOM	1692	CG	LEU	880	33.089	-5.838	1.939	1.00	18.50
ATOM	1693	CD1	LEU	880	33.310	-6.886	0.855	1.00	19.38
ATOM	1694	CD2	LEU	880	32.159	-4.762	1.477	1.00	18.07
ATOM	1695	C	LEU	880	34.529	-7.496	4.136	1.00	20.40
ATOM	1696	O	LEU	880	35.513	-7.723	3.453	1.00	21.41
ATOM	1697	N	LEU	881	34.602	-7.040	5.376	1.00	20.90
ATOM	1698	CA	LEU	881	35.882	-6.723	6.011	1.00	20.84
ATOM	1699	CB	LEU	881	35.651	-6.055	7.364	1.00	19.23
ATOM	1700	CG	LEU	881	36.989	-5.773	8.031	1.00	19.26
ATOM	1701	CD1	LEU	881	37.662	-4.593	7.350	1.00	19.67
ATOM	1702	CD2	LEU	881	36.810	-5.514	9.500	1.00	18.92
ATOM	1703	C	LEU	881	36.818	-7.923	6.188	1.00	21.55
ATOM	1704	O	LEU	881	38.055	-7.806	6.107	1.00	21.03
ATOM	1705	N	ILE	882	36.230	-9.063	6.492	1.00	22.39
ATOM	1706	CA	ILE	882	37.013	-10.265	6.671	1.00	23.63
ATOM	1707	CB	ILE	882	36.136	-11.390	7.248	1.00	23.00
ATOM	1708	CG2	ILE	882	36.855	-12.729	7.185	1.00	22.75
ATOM	1709	CG1	ILE	882	35.749	-11.006	8.675	1.00	22.91
ATOM	1710	CD1	ILE	882	36.922	-10.412	9.491	1.00	22.94
ATOM	1711	C	ILE	882	37.668	-10.643	5.340	1.00	24.48
ATOM	1712	O	ILE	882	38.859	-10.953	5.290	1.00	24.23
ATOM	1713	N	LYS	883	36.908	-10.541	4.256	1.00	25.73
ATOM	1714	CA	LYS	883	37.441	-10.868	2.945	1.00	28.25
ATOM	1715	CB	LYS	883	36.492	-11.820	2.211	1.00	27.47
ATOM	1716	CG	LYS	883	35.140	-11.240	1.932	1.00	27.17
ATOM	1717	CD	LYS	883	34.293	-12.163	1.109	1.00	27.60
ATOM	1718	CE	LYS	883	32.926	-11.544	0.899	1.00	28.94
ATOM	1719	NZ	LYS	883	32.036	-12.319	-0.003	1.00	29.99
ATOM	1720	C	LYS	883	37.749	-9.657	2.061	1.00	30.08
ATOM	1721	O	LYS	883	37.823	-9.790	0.841	1.00	30.81
ATOM	1722	N	SER	884	37.976	-8.495	2.672	1.00	32.24
ATOM	1723	CA	SER	884	38.268	-7.260	1.938	1.00	33.66
ATOM	1724	CB	SER	884	38.440	-6.106	2.921	1.00	32.96
ATOM	1725	OG	SER	884	39.466	-6.384	3.856	1.00	32.02
ATOM	1726	C	SER	884	39.500	-7.349	1.042	1.00	35.48
ATOM	1727	O	SER	884	39.491	-6.867	-0.087	1.00	35.08
ATOM	1728	N	HIS	885	40.557	-7.969	1.556	1.00	38.15
ATOM	1729	CA	HIS	885	41.815	-8.138	0.824	1.00	40.84
ATOM	1730	CB	HIS	885	42.882	-8.688	1.789	1.00	43.70
ATOM	1731	CG	HIS	885	44.032	-9.392	1.124	1.00	47.44
ATOM	1732	CD2	HIS	885	44.240	-10.707	0.860	1.00	49.14

ATOM	1733	ND1	HIS	885	45.172	-8.737	0.704	1.00	49.20
ATOM	1734	CE1	HIS	885	46.034	-9.615	0.217	1.00	49.74
ATOM	1735	NE2	HIS	885	45.493	-10.818	0.300	1.00	50.17
ATOM	1736	C	HIS	885	41.682	-9.017	-0.432	1.00	41.12
ATOM	1737	O	HIS	885	42.563	-9.010	-1.288	1.00	41.51
ATOM	1738	N	MET	886	40.586	-9.762	-0.544	1.00	41.14
ATOM	1739	CA	MET	886	40.372	-10.639	-1.686	1.00	41.17
ATOM	1740	CB	MET	886	39.859	-11.989	-1.212	1.00	43.08
ATOM	1741	CG	MET	886	40.928	-12.860	-0.584	1.00	45.59
ATOM	1742	SD	MET	886	40.175	-14.113	0.457	1.00	50.78
ATOM	1743	CE	MET	886	39.069	-14.971	-0.725	1.00	48.51
ATOM	1744	C	MET	886	39.455	-10.074	-2.761	1.00	40.68
ATOM	1745	O	MET	886	39.535	-10.476	-3.923	1.00	41.66
ATOM	1746	N	VAL	887	38.542	-9.193	-2.370	1.00	39.25
ATOM	1747	CA	VAL	887	37.637	-8.565	-3.333	1.00	37.55
ATOM	1748	CB	VAL	887	36.187	-8.459	-2.802	1.00	37.19
ATOM	1749	CG1	VAL	887	35.526	-9.828	-2.756	1.00	37.49
ATOM	1750	CG2	VAL	887	36.175	-7.817	-1.429	1.00	36.99
ATOM	1751	C	VAL	887	38.145	-7.168	-3.702	1.00	37.08
ATOM	1752	O	VAL	887	37.484	-6.444	-4.442	1.00	37.26
ATOM	1753	N	SER	888	39.320	-6.809	-3.188	1.00	35.90
ATOM	1754	CA	SER	888	39.955	-5.515	-3.437	1.00	35.05
ATOM	1755	CB	SER	888	40.231	-5.342	-4.929	1.00	35.29
ATOM	1756	OG	SER	888	41.335	-6.133	-5.326	1.00	36.74
ATOM	1757	C	SER	888	39.216	-4.290	-2.898	1.00	34.27
ATOM	1758	O	SER	888	39.402	-3.179	-3.396	1.00	34.78
ATOM	1759	N	VAL	889	38.391	-4.485	-1.875	1.00	32.78
ATOM	1760	CA	VAL	889	37.636	-3.386	-1.283	1.00	31.50
ATOM	1761	CB	VAL	889	36.244	-3.857	-0.772	1.00	30.79
ATOM	1762	CG1	VAL	889	35.509	-2.729	-0.055	1.00	30.12
ATOM	1763	CG2	VAL	889	35.410	-4.364	-1.903	1.00	30.08
ATOM	1764	C	VAL	889	38.410	-3.002	-0.064	1.00	31.36
ATOM	1765	O	VAL	889	38.855	-3.895	0.648	1.00	32.20
ATOM	1766	N	ASP	890	38.692	-1.724	0.156	1.00	31.10
ATOM	1767	CA	ASP	890	39.364	-1.428	1.414	1.00	30.80
ATOM	1768	CB	ASP	890	40.849	-1.093	1.296	1.00	33.89
ATOM	1769	CG	ASP	890	41.720	-1.949	2.261	1.00	35.96
ATOM	1770	OD1	ASP	890	41.248	-2.314	3.373	1.00	35.86
ATOM	1771	OD2	ASP	890	42.882	-2.260	1.901	1.00	37.33
ATOM	1772	C	ASP	890	38.629	-0.493	2.326	1.00	28.51
ATOM	1773	O	ASP	890	37.889	0.379	1.889	1.00	27.96
ATOM	1774	N	PHE	891	38.761	-0.782	3.610	1.00	26.20
ATOM	1775	CA	PHE	891	38.096	-0.045	4.661	1.00	24.15
ATOM	1776	CB	PHE	891	37.595	-1.027	5.732	1.00	20.51
ATOM	1777	CG	PHE	891	36.501	-1.937	5.259	1.00	16.33
ATOM	1778	CD1	PHE	891	36.741	-2.892	4.288	1.00	15.42
ATOM	1779	CD2	PHE	891	35.230	-1.826	5.773	1.00	14.37
ATOM	1780	CE1	PHE	891	35.720	-3.730	3.832	1.00	13.60
ATOM	1781	CE2	PHE	891	34.220	-2.648	5.335	1.00	14.04
ATOM	1782	CZ	PHE	891	34.467	-3.607	4.353	1.00	13.43
ATOM	1783	C	PHE	891	39.036	0.942	5.305	1.00	24.58
ATOM	1784	O	PHE	891	40.150	0.574	5.695	1.00	25.30
ATOM	1785	N	PRO	892	38.603	2.209	5.437	1.00	23.93
ATOM	1786	CD	PRO	892	37.376	2.811	4.909	1.00	22.44
ATOM	1787	CA	PRO	892	39.441	3.234	6.060	1.00	23.41
ATOM	1788	CB	PRO	892	38.582	4.485	5.940	1.00	23.21
ATOM	1789	CG	PRO	892	37.796	4.241	4.748	1.00	23.19
ATOM	1790	C	PRO	892	39.655	2.866	7.520	1.00	23.31
ATOM	1791	O	PRO	892	38.887	2.090	8.078	1.00	22.72
ATOM	1792	N	GLU	893	40.619	3.517	8.157	1.00	24.55
ATOM	1793	CA	GLU	893	40.984	3.267	9.555	1.00	26.50
ATOM	1794	CB	GLU	893	41.885	4.385	10.072	1.00	28.90

ATOM	1795	CG	GLU	893	42.329	4.192	11.509	1.00	33.98
ATOM	1796	CD	GLU	893	42.441	5.498	12.280	1.00	37.38
ATOM	1797	OE1	GLU	893	43.356	6.292	11.955	1.00	39.69
ATOM	1798	OE2	GLU	893	41.624	5.729	13.216	1.00	39.34
ATOM	1799	C	GLU	893	39.859	3.054	10.563	1.00	26.24
ATOM	1800	O	GLU	893	39.750	1.992	11.180	1.00	27.29
ATOM	1801	N	MET	894	39.052	4.078	10.782	1.00	26.07
ATOM	1802	CA	MET	894	37.968	3.974	11.744	1.00	26.28
ATOM	1803	CB	MET	894	37.313	5.337	11.954	1.00	28.30
ATOM	1804	CG	MET	894	38.256	6.389	12.509	1.00	32.56
ATOM	1805	SD	MET	894	38.847	5.925	14.144	1.00	38.01
ATOM	1806	CE	MET	894	37.260	5.830	15.037	1.00	35.95
ATOM	1807	C	MET	894	36.927	2.918	11.393	1.00	24.69
ATOM	1808	O	MET	894	36.337	2.311	12.287	1.00	24.64
ATOM	1809	N	MET	895	36.662	2.743	10.102	1.00	23.64
ATOM	1810	CA	MET	895	35.705	1.738	9.645	1.00	22.83
ATOM	1811	CB	MET	895	35.487	1.824	8.135	1.00	21.32
ATOM	1812	CG	MET	895	34.669	3.006	7.693	1.00	21.17
ATOM	1813	SD	MET	895	33.044	3.064	8.432	1.00	20.56
ATOM	1814	CE	MET	895	32.088	2.305	7.205	1.00	22.81
ATOM	1815	C	MET	895	36.171	0.328	10.032	1.00	22.26
ATOM	1816	O	MET	895	35.469	-0.383	10.714	1.00	22.26
ATOM	1817	N	ALA	896	37.362	-0.066	9.616	1.00	22.06
ATOM	1818	CA	ALA	896	37.867	-1.378	9.953	1.00	22.36
ATOM	1819	CB	ALA	896	39.243	-1.588	9.350	1.00	22.56
ATOM	1820	C	ALA	896	37.914	-1.581	11.460	1.00	22.96
ATOM	1821	O	ALA	896	37.520	-2.630	11.947	1.00	23.87
ATOM	1822	N	GLU	897	38.377	-0.586	12.212	1.00	23.92
ATOM	1823	CA	GLU	897	38.455	-0.724	13.666	1.00	24.05
ATOM	1824	CB	GLU	897	39.128	0.502	14.313	1.00	25.98
ATOM	1825	CG	GLU	897	39.288	0.390	15.841	1.00	27.50
ATOM	1826	CD	GLU	897	39.150	1.718	16.555	1.00	27.88
ATOM	1827	OE1	GLU	897	40.150	2.453	16.674	1.00	29.49
ATOM	1828	OE2	GLU	897	38.036	2.018	17.013	1.00	29.22
ATOM	1829	C	GLU	897	37.076	-0.901	14.276	1.00	22.80
ATOM	1830	O	GLU	897	36.873	-1.774	15.094	1.00	22.95
ATOM	1831	N	ILE	898	36.129	-0.071	13.884	1.00	22.19
ATOM	1832	CA	ILE	898	34.801	-0.178	14.459	1.00	21.88
ATOM	1833	CB	ILE	898	33.940	1.077	14.196	1.00	21.85
ATOM	1834	CG2	ILE	898	32.478	0.836	14.587	1.00	22.66
ATOM	1835	CG1	ILE	898	34.438	2.233	15.043	1.00	22.82
ATOM	1836	CD1	ILE	898	33.490	3.390	15.019	1.00	23.11
ATOM	1837	C	ILE	898	34.080	-1.398	13.968	1.00	20.49
ATOM	1838	O	ILE	898	33.228	-1.917	14.656	1.00	21.90
ATOM	1839	N	ILE	899	34.410	-1.860	12.781	1.00	19.59
ATOM	1840	CA	ILE	899	33.747	-3.027	12.248	1.00	19.42
ATOM	1841	CB	ILE	899	33.758	-3.014	10.706	1.00	19.12
ATOM	1842	CG2	ILE	899	33.095	-4.285	10.157	1.00	18.71
ATOM	1843	CG1	ILE	899	32.987	-1.786	10.187	1.00	18.56
ATOM	1844	CD1	ILE	899	33.054	-1.588	8.683	1.00	15.05
ATOM	1845	C	ILE	899	34.305	-4.338	12.832	1.00	19.02
ATOM	1846	O	ILE	899	33.571	-5.300	12.982	1.00	19.98
ATOM	1847	N	SER	900	35.565	-4.344	13.233	1.00	19.03
ATOM	1848	CA	SER	900	36.177	-5.518	13.822	1.00	19.74
ATOM	1849	CB	SER	900	37.614	-5.631	13.340	1.00	19.62
ATOM	1850	OG	SER	900	38.368	-4.478	13.683	1.00	22.08
ATOM	1851	C	SER	900	36.135	-5.502	15.355	1.00	20.48
ATOM	1852	O	SER	900	36.352	-6.521	16.010	1.00	21.19
ATOM	1853	N	VAL	901	35.866	-4.346	15.939	1.00	20.99
ATOM	1854	CA	VAL	901	35.808	-4.235	17.396	1.00	20.43
ATOM	1855	CB	VAL	901	36.705	-3.074	17.927	1.00	20.22
ATOM	1856	CG1	VAL	901	36.407	-2.785	19.382	1.00	20.37

ATOM	1857	CG2	VAL	901	38.168	-3.436	17.782	1.00	18.81
ATOM	1858	C	VAL	901	34.397	-4.087	17.935	1.00	20.42
ATOM	1859	O	VAL	901	33.999	-4.823	18.841	1.00	21.68
ATOM	1860	N	GLN	902	33.614	-3.187	17.350	1.00	19.34
ATOM	1861	CA	GLN	902	32.264	-2.957	17.828	1.00	17.55
ATOM	1862	CB	GLN	902	31.929	-1.476	17.735	1.00	19.32
ATOM	1863	CG	GLN	902	32.952	-0.579	18.371	1.00	20.82
ATOM	1864	CD	GLN	902	33.089	-0.776	19.861	1.00	23.15
ATOM	1865	OE1	GLN	902	32.211	-1.336	20.528	1.00	23.22
ATOM	1866	NE2	GLN	902	34.197	-0.288	20.404	1.00	25.36
ATOM	1867	C	GLN	902	31.145	-3.766	17.207	1.00	16.24
ATOM	1868	O	GLN	902	30.337	-4.326	17.938	1.00	15.40
ATOM	1869	N	VAL	903	31.075	-3.810	15.872	1.00	15.79
ATOM	1870	CA	VAL	903	30.025	-4.552	15.144	1.00	15.22
ATOM	1871	CB	VAL	903	30.195	-4.461	13.594	1.00	14.30
ATOM	1872	CG1	VAL	903	29.159	-5.314	12.883	1.00	13.20
ATOM	1873	CG2	VAL	903	30.012	-3.005	13.147	1.00	14.90
ATOM	1874	C	VAL	903	29.860	-6.010	15.605	1.00	14.74
ATOM	1875	O	VAL	903	28.732	-6.489	15.693	1.00	14.48
ATOM	1876	N	PRO	904	30.976	-6.729	15.893	1.00	14.65
ATOM	1877	CD	PRO	904	32.377	-6.425	15.571	1.00	13.72
ATOM	1878	CA	PRO	904	30.884	-8.122	16.356	1.00	15.80
ATOM	1879	CB	PRO	904	32.350	-8.481	16.602	1.00	15.45
ATOM	1880	CG	PRO	904	33.014	-7.830	15.512	1.00	14.60
ATOM	1881	C	PRO	904	30.053	-8.206	17.632	1.00	16.77
ATOM	1882	O	PRO	904	29.151	-9.039	17.713	1.00	18.38
ATOM	1883	N	LYS	905	30.286	-7.295	18.589	1.00	17.00
ATOM	1884	CA	LYS	905	29.525	-7.292	19.830	1.00	16.34
ATOM	1885	CB	LYS	905	29.866	-6.085	20.668	1.00	18.17
ATOM	1886	CG	LYS	905	31.293	-6.007	21.132	1.00	19.96
ATOM	1887	CD	LYS	905	31.464	-4.733	21.947	1.00	22.09
ATOM	1888	CE	LYS	905	32.911	-4.429	22.276	1.00	23.59
ATOM	1889	NZ	LYS	905	33.003	-3.173	23.083	1.00	27.13
ATOM	1890	C	LYS	905	28.039	-7.273	19.546	1.00	15.58
ATOM	1891	O	LYS	905	27.251	-7.817	20.297	1.00	15.43
ATOM	1892	N	ILE	906	27.647	-6.620	18.466	1.00	15.71
ATOM	1893	CA	ILE	906	26.239	-6.554	18.086	1.00	15.74
ATOM	1894	CB	ILE	906	25.991	-5.423	17.030	1.00	14.76
ATOM	1895	CG2	ILE	906	24.527	-5.427	16.565	1.00	13.47
ATOM	1896	CG1	ILE	906	26.358	-4.051	17.611	1.00	13.40
ATOM	1897	CD1	ILE	906	26.021	-2.876	16.686	1.00	13.18
ATOM	1898	C	ILE	906	25.800	-7.899	17.478	1.00	17.05
ATOM	1899	O	ILE	906	24.759	-8.471	17.834	1.00	16.35
ATOM	1900	N	LEU	907	26.609	-8.385	16.539	1.00	17.95
ATOM	1901	CA	LEU	907	26.348	-9.631	15.827	1.00	17.64
ATOM	1902	CB	LEU	907	27.331	-9.787	14.659	1.00	15.32
ATOM	1903	CG	LEU	907	27.338	-8.653	13.632	1.00	14.36
ATOM	1904	CD1	LEU	907	28.382	-8.885	12.557	1.00	12.28
ATOM	1905	CD2	LEU	907	25.947	-8.531	13.029	1.00	13.60
ATOM	1906	C	LEU	907	26.386	-10.858	16.747	1.00	18.93
ATOM	1907	O	LEU	907	25.756	-11.860	16.437	1.00	20.36
ATOM	1908	N	SER	908	27.097	-10.805	17.868	1.00	19.02
ATOM	1909	CA	SER	908	27.103	-11.947	18.772	1.00	19.60
ATOM	1910	CB	SER	908	28.469	-12.099	19.407	1.00	19.21
ATOM	1911	OG	SER	908	28.811	-10.944	20.135	1.00	19.20
ATOM	1912	C	SER	908	26.027	-11.844	19.867	1.00	20.23
ATOM	1913	O	SER	908	25.946	-12.709	20.752	1.00	20.86
ATOM	1914	N	GLY	909	25.208	-10.791	19.812	1.00	19.30
ATOM	1915	CA	GLY	909	24.169	-10.603	20.817	1.00	18.22
ATOM	1916	C	GLY	909	24.533	-9.859	22.102	1.00	16.28
ATOM	1917	O	GLY	909	23.711	-9.712	22.987	1.00	16.09
ATOM	1918	N	LYS	910	25.773	-9.422	22.236	1.00	16.37

	ATOM	1919	CA	LYS	910	26.166	-8.670	23.411	1.00	17.37
	ATOM	1920	CB	LYS	910	27.665	-8.464	23.403	1.00	17.13
	ATOM	1921	CG	LYS	910	28.418	-9.703	23.684	1.00	16.32
	ATOM	1922	CD	LYS	910	29.860	-9.370	23.896	1.00	17.48
5	ATOM	1923	CE	LYS	910	30.577	-10.534	24.482	1.00	17.90
	ATOM	1924	NZ	LYS	910	32.055	-10.284	24.502	1.00	19.93
	ATOM	1925	C	LYS	910	25.472	-7.296	23.532	1.00	18.68
	ATOM	1926	O	LYS	910	25.250	-6.797	24.640	1.00	19.51
	ATOM	1927	N	VAL	911	25.219	-6.641	22.397	1.00	18.99
10	ATOM	1928	CA	VAL	911	24.545	-5.341	22.396	1.00	17.49
	ATOM	1929	CB	VAL	911	25.501	-4.130	22.041	1.00	17.52
	ATOM	1930	CG1	VAL	911	26.928	-4.550	22.019	1.00	15.48
	ATOM	1931	CG2	VAL	911	25.094	-3.412	20.788	1.00	15.48
	ATOM	1932	C	VAL	911	23.379	-5.475	21.458	1.00	17.48
15	ATOM	1933	O	VAL	911	23.504	-6.015	20.358	1.00	17.40
	ATOM	1934	N	LYS	912	22.219	-5.032	21.896	1.00	17.96
	ATOM	1935	CA	LYS	912	21.057	-5.210	21.072	1.00	19.32
	ATOM	1936	CB	LYS	912	20.189	-6.325	21.672	1.00	21.17
	ATOM	1937	CG	LYS	912	19.261	-5.889	22.811	1.00	25.24
20	ATOM	1938	CD	LYS	912	19.998	-5.297	24.030	1.00	26.63
	ATOM	1939	CE	LYS	912	19.509	-3.871	24.370	1.00	26.56
	ATOM	1940	NZ	LYS	912	18.028	-3.782	24.457	1.00	27.08
	ATOM	1941	C	LYS	912	20.262	-3.943	20.903	1.00	19.72
	ATOM	1942	O	LYS	912	20.437	-2.985	21.651	1.00	19.46
25	ATOM	1943	N	PRO	913	19.463	-3.877	19.841	1.00	20.13
	ATOM	1944	CD	PRO	913	19.437	-4.660	18.599	1.00	20.38
	ATOM	1945	CA	PRO	913	18.693	-2.665	19.683	1.00	20.09
	ATOM	1946	CB	PRO	913	18.174	-2.780	18.259	1.00	20.97
	ATOM	1947	CG	PRO	913	18.127	-4.240	18.017	1.00	21.02
30	ATOM	1948	C	PRO	913	17.555	-2.665	20.658	1.00	20.77
	ATOM	1949	O	PRO	913	17.108	-3.719	21.120	1.00	20.82
	ATOM	1950	N	ILE	914	17.094	-1.460	20.972	1.00	20.62
	ATOM	1951	CA	ILE	914	15.965	-1.262	21.846	1.00	18.90
	ATOM	1952	CB	ILE	914	16.119	0.012	22.659	1.00	17.34
35	ATOM	1953	CG2	ILE	914	14.953	0.149	23.589	1.00	15.42
	ATOM	1954	CG1	ILE	914	17.445	-0.022	23.418	1.00	16.40
	ATOM	1955	CD1	ILE	914	17.794	1.261	24.098	1.00	15.82
	ATOM	1956	C	ILE	914	14.823	-1.093	20.858	1.00	19.73
	ATOM	1957	O	ILE	914	14.946	-0.313	19.909	1.00	20.71
40	ATOM	1958	N	TYR	915	13.774	-1.908	20.995	1.00	19.80
	ATOM	1959	CA	TYR	915	12.622	-1.823	20.105	1.00	19.03
	ATOM	1960	CB	TYR	915	12.194	-3.193	19.566	1.00	18.88
	ATOM	1961	CG	TYR	915	13.072	-3.773	18.505	1.00	18.76
	ATOM	1962	CD1	TYR	915	14.096	-4.640	18.832	1.00	19.63
45	ATOM	1963	CE1	TYR	915	14.923	-5.170	17.853	1.00	21.76
	ATOM	1964	CD2	TYR	915	12.881	-3.457	17.173	1.00	19.64
	ATOM	1965	CE2	TYR	915	13.698	-3.989	16.177	1.00	20.92
	ATOM	1966	CZ	TYR	915	14.721	-4.839	16.531	1.00	21.98
	ATOM	1967	OH	TYR	915	15.592	-5.314	15.577	1.00	25.00
50	ATOM	1968	C	TYR	915	11.468	-1.273	20.882	1.00	18.68
	ATOM	1969	O	TYR	915	11.340	-1.494	22.080	1.00	18.72
	ATOM	1970	N	PHE	916	10.621	-0.543	20.194	1.00	18.68
	ATOM	1971	CA	PHE	916	9.456	-0.019	20.836	1.00	19.66
	ATOM	1972	CB	PHE	916	8.898	1.145	20.042	1.00	17.07
55	ATOM	1973	CG	PHE	916	9.567	2.411	20.335	1.00	14.89
	ATOM	1974	CD1	PHE	916	9.377	3.034	21.561	1.00	16.16
	ATOM	1975	CD2	PHE	916	10.393	2.992	19.407	1.00	16.16
	ATOM	1976	CE1	PHE	916	10.010	4.225	21.854	1.00	14.78
	ATOM	1977	CE2	PHE	916	11.028	4.183	19.689	1.00	16.01
60	ATOM	1978	CZ	PHE	916	10.836	4.800	20.916	1.00	15.28
	ATOM	1979	C	PHE	916	8.451	-1.148	20.868	1.00	21.60
	ATOM	1980	O	PHE	916	7.862	-1.434	21.910	1.00	22.04

	ATOM	1981	N	HIS	917	8.300	-1.804	19.718	1.00	22.86
	ATOM	1982	CA	HIS	917	7.354	-2.899	19.543	1.00	24.45
	ATOM	1983	CB	HIS	917	6.549	-2.696	18.258	1.00	23.60
	ATOM	1984	CG	HIS	917	5.921	-1.347	18.153	1.00	21.90
5	ATOM	1985	CD2	HIS	917	6.440	-0.153	17.787	1.00	21.97
	ATOM	1986	ND1	HIS	917	4.614	-1.109	18.504	1.00	21.41
	ATOM	1987	CE1	HIS	917	4.350	0.178	18.360	1.00	22.05
	ATOM	1988	NE2	HIS	917	5.446	0.783	17.929	1.00	21.26
	ATOM	1989	C	HIS	917	8.077	-4.225	19.477	1.00	25.83
10	ATOM	1990	OT1	HIS	917	9.185	-4.257	18.908	1.00	27.53
	ATOM	1991	OT2	HIS	917	7.525	-5.225	19.988	1.00	29.26
	ATOM	1992	C1	DHT	920	27.685	5.199	4.565	1.00	13.59
	ATOM	1993	C2	DHT	920	26.814	6.485	4.636	1.00	12.55
	ATOM	1994	C3	DHT	920	25.484	6.280	3.944	1.00	12.58
15	ATOM	1995	O3	DHT	920	24.904	7.249	3.448	1.00	11.99
	ATOM	1996	C4	DHT	920	24.887	4.964	3.857	1.00	13.18
	ATOM	1997	C5	DHT	920	25.464	3.903	4.357	1.00	13.98
	ATOM	1998	C6	DHT	920	24.727	2.560	4.241	1.00	14.79
	ATOM	1999	C7	DHT	920	25.613	1.454	3.609	1.00	14.79
20	ATOM	2000	C8	DHT	920	26.955	1.303	4.359	1.00	15.54
	ATOM	2001	C9	DHT	920	27.708	2.656	4.279	1.00	14.37
	ATOM	2002	C10	DHT	920	26.943	3.876	4.949	1.00	14.56
	ATOM	2003	C11	DHT	920	29.161	2.525	4.830	1.00	14.73
	ATOM	2004	C12	DHT	920	29.951	1.344	4.192	1.00	14.11
25	ATOM	2005	C13	DHT	920	29.194	-0.010	4.339	1.00	15.34
	ATOM	2006	C14	DHT	920	27.784	0.212	3.680	1.00	15.67
	ATOM	2007	C15	DHT	920	27.178	-1.232	3.647	1.00	15.64
	ATOM	2008	C16	DHT	920	28.435	-2.118	3.310	1.00	15.37
	ATOM	2009	C17	DHT	920	29.679	-1.189	3.426	1.00	14.87
30	ATOM	2010	C18	DHT	920	29.107	-0.450	5.847	1.00	14.67
	ATOM	2011	C19	DHT	920	26.781	3.770	6.524	1.00	13.94
	ATOM	2012	O20	DHT	920	30.910	-1.918	3.981	1.00	16.20
	ATOM	2013	O	HOH	921	16.187	17.463	26.217	1.00	26.98
	ATOM	2014	O	HOH	922	19.878	17.183	14.290	1.00	13.49
35	ATOM	2015	O	HOH	923	18.473	14.908	14.407	1.00	6.52
	ATOM	2016	O	HOH	924	29.144	18.703	11.673	1.00	37.40
	ATOM	2017	O	HOH	925	27.076	19.321	12.893	1.00	18.76
	ATOM	2018	O	HOH	926	23.789	12.817	9.649	1.00	33.78
	ATOM	2019	O	HOH	927	25.400	14.577	5.432	1.00	19.79
40	ATOM	2020	O	HOH	928	23.015	12.473	12.245	1.00	14.03
	ATOM	2021	O	HOH	929	25.209	14.445	2.442	1.00	19.95
	ATOM	2022	O	HOH	930	34.235	16.490	0.235	1.00	41.09
	ATOM	2023	O	HOH	931	31.687	16.720	1.143	1.00	22.88
	ATOM	2024	O	HOH	932	26.451	12.094	2.237	1.00	8.25
45	ATOM	2025	O	HOH	933	11.606	-0.191	-7.963	1.00	46.13
	ATOM	2026	O	HOH	934	13.798	0.894	17.657	1.00	15.30
	ATOM	2027	O	HOH	935	15.475	2.114	16.386	1.00	12.01
	ATOM	2028	O	HOH	936	8.514	-2.110	12.665	1.00	21.79
	ATOM	2029	O	HOH	937	23.094	0.783	14.094	1.00	10.94
50	ATOM	2030	O	HOH	938	23.758	-13.306	5.541	1.00	40.43
	ATOM	2031	O	HOH	939	22.933	-11.472	10.611	1.00	31.03
	ATOM	2032	O	HOH	940	26.094	-11.914	5.354	1.00	51.71
	ATOM	2033	O	HOH	941	10.995	-6.843	16.294	1.00	29.91
	ATOM	2034	O	HOH	942	23.088	7.362	-10.811	1.00	30.10
55	ATOM	2035	O	HOH	943	26.671	9.139	-8.686	1.00	38.12
	ATOM	2036	O	HOH	946	35.410	-8.438	-7.084	1.00	42.68
	ATOM	2037	O	HOH	947	10.842	24.253	21.391	1.00	43.09
	ATOM	2038	O	HOH	948	15.704	21.095	27.707	1.00	54.35
	ATOM	2039	O	HOH	949	1.671	16.382	5.866	1.00	24.50
60	ATOM	2040	O	HOH	950	8.009	20.744	8.572	1.00	36.16
	ATOM	2041	O	HOH	951	29.490	17.190	30.961	1.00	56.26
	ATOM	2042	O	HOH	952	23.829	-12.134	25.596	1.00	39.41

ATOM	2043	O	HOH	953	42.457	5.523	7.132	1.00	28.93
ATOM	2044	O	HOH	954	41.318	2.323	2.406	1.00	38.22
ATOM	2045	O	HOH	955	25.857	7.152	30.722	1.00	18.97
ATOM	2046	O	HOH	956	18.191	16.505	27.701	1.00	29.01
ATOM	2047	O	HOH	957	14.018	2.408	20.246	1.00	18.75
ATOM	2048	O	HOH	958	14.651	4.006	17.873	1.00	21.70
ATOM	2049	O	HOH	959	5.786	11.770	25.499	1.00	35.58
ATOM	2050	O	HOH	960	2.694	19.497	9.834	1.00	25.35
ATOM	2051	O	HOH	961	0.334	6.151	20.624	1.00	27.66
ATOM	2052	O	HOH	962	-2.677	2.639	17.420	1.00	35.67
ATOM	2053	O	HOH	963	0.868	8.543	25.138	1.00	43.49
ATOM	2054	O	HOH	964	-8.085	7.667	23.358	1.00	40.82
ATOM	2055	O	HOH	965	6.749	1.200	9.766	1.00	24.57
ATOM	2056	O	HOH	966	-0.636	8.734	6.585	1.00	40.09
ATOM	2057	O	HOH	967	22.487	-4.734	14.335	1.00	28.04
ATOM	2058	O	HOH	968	18.615	17.070	7.167	1.00	23.83
ATOM	2059	O	HOH	969	10.049	19.612	2.716	1.00	28.02
ATOM	2060	O	HOH	970	26.829	21.030	22.736	1.00	25.40
ATOM	2061	O	HOH	971	23.684	9.361	5.898	1.00	24.06
ATOM	2062	O	HOH	972	23.124	15.837	0.189	1.00	29.07
ATOM	2063	O	HOH	973	34.079	8.287	19.446	1.00	34.35
ATOM	2064	O	HOH	974	37.522	2.898	1.092	1.00	22.39
ATOM	2065	O	HOH	975	21.838	14.392	5.445	1.00	20.42
ATOM	2066	O	HOH	976	16.106	-10.859	0.784	1.00	48.09
ATOM	2067	O	HOH	977	11.295	27.231	20.742	1.00	24.50
ATOM	2068	O	HOH	978	21.562	-7.923	18.100	1.00	34.94
ATOM	2069	O	HOH	979	41.647	-2.962	5.907	1.00	41.33
ATOM	2070	O	HOH	981	12.897	22.682	24.938	1.00	44.10
ATOM	2071	O	HOH	982	33.709	13.619	-5.931	1.00	26.84
ATOM	2072	O	HOH	983	0.019	-4.834	14.164	1.00	36.91
ATOM	2073	O	HOH	984	39.563	3.365	-2.334	1.00	36.56
ATOM	2074	O	HOH	985	16.244	18.091	7.952	1.00	25.52
ATOM	2075	O	HOH	986	13.038	13.790	19.688	1.00	21.93
ATOM	2076	O	HOH	987	22.095	3.621	21.834	1.00	19.27
ATOM	2077	O	HOH	988	2.516	2.235	3.905	1.00	30.91
ATOM	2078	O	HOH	989	2.950	1.064	1.716	1.00	31.16
ATOM	2079	O	HOH	990	5.186	-1.082	5.207	1.00	26.66
ATOM	2080	O	HOH	991	-0.310	15.229	24.529	1.00	28.42
ATOM	2081	O	HOH	992	-6.181	9.210	18.935	1.00	37.84
ATOM	2082	O	HOH	993	17.508	26.662	14.814	1.00	30.32
ATOM	2083	O	HOH	994	17.401	31.211	13.007	1.00	30.57
ATOM	2084	O	HOH	995	21.268	22.961	10.009	1.00	33.92
ATOM	2085	O	HOH	996	26.335	12.379	6.567	1.00	36.58
ATOM	2086	O	HOH	997	33.730	15.077	4.345	1.00	24.42
ATOM	2087	O	HOH	998	28.576	2.290	-15.305	1.00	30.54
ATOM	2088	O	HOH	999	33.926	-5.402	-13.979	1.00	48.01
ATOM	2089	O	HOH	1000	31.878	-6.250	-10.283	1.00	38.45
ATOM	2090	O	HOH	1021	30.673	18.487	18.256	1.00	34.16
ATOM	2091	O	HOH	1022	35.035	20.192	15.084	1.00	37.70
ATOM	2092	O	HOH	1023	32.791	17.836	19.423	1.00	35.34
ATOM	2093	O	HOH	1024	22.587	-14.097	7.907	1.00	30.71
ATOM	2094	O	HOH	1025	29.778	-9.620	-0.255	1.00	24.68
ATOM	2095	O	HOH	1026	25.904	17.949	24.176	1.00	16.80
ATOM	2096	O	HOH	1027	33.066	-13.092	7.455	1.00	20.84
ATOM	2097	O	HOH	1028	31.787	15.265	28.988	1.00	32.80
ATOM	2098	O	HOH	1029	27.029	0.835	13.994	1.00	20.01
ATOM	2099	O	HOH	1030	20.499	2.720	16.384	1.00	31.66
ATOM	2100	O	HOH	1031	10.991	16.858	-1.085	1.00	30.58
ATOM	2101	O	HOH	1032	7.904	10.344	-5.081	1.00	41.55
ATOM	2102	O	HOH	1033	12.570	3.398	-10.099	1.00	26.95
ATOM	2103	O	HOH	1034	17.128	3.214	-10.962	1.00	22.24
ATOM	2104	O	HOH	1035	17.056	1.547	-4.553	1.00	26.98

ATOM	2105	O	HOH	1036	11.020	0.892	6.595	1.00	25.24
ATOM	2106	O	HOH	1037	3.092	-1.135	-0.025	1.00	27.44
ATOM	2107	O	HOH	1038	24.006	5.653	35.765	1.00	34.54
ATOM	2108	O	HOH	1039	29.738	0.950	27.680	1.00	26.47
ATOM	2109	O	HOH	1040	1.507	8.706	22.315	1.00	36.26
ATOM	2110	O	HOH	1041	10.755	-4.751	9.776	1.00	27.77
ATOM	2111	O	HOH	1042	20.223	-3.560	14.440	1.00	25.10
ATOM	2112	O	HOH	1043	30.147	-9.103	2.467	1.00	26.08
ATOM	2113	O	HOH	1044	28.518	-12.565	-5.152	1.00	28.96
ATOM	2114	O	HOH	1045	39.044	7.751	17.961	1.00	38.02
ATOM	2115	O	HOH	1046	37.030	10.428	20.994	1.00	37.73
ATOM	2116	O	HOH	1047	7.847	-2.227	15.270	1.00	24.79
ATOM	2117	O	HOH	1048	9.958	-5.351	21.522	1.00	40.62
ATOM	2118	O	HOH	1049	6.839	-6.928	22.567	1.00	30.96

We claim:

1. A crystal of an AR-LBD comprising:
    a) an AR-LBD and an AR-LBD ligand or
    b) an AR-LBD without an AR-LBD ligand;

wherein said crystal diffracts to at least 3 angstrom resolution and has a crystal stability within 5% of its unit cell dimensions.

2. The crystal of claim 1 wherein said AR-LBD has at least 200 amino acids.
3. The crystal of claim 1, wherein said AR-LBD is the AR amino acid sequence 672 to 917 of rat AR
4. The crystal of claim 1, wherein said AR-LBD is the AR amino acid sequence 672 to 917 of human AR.
5. The crystal of claim 1 wherein the crystal comprises an AR-LBD and an AR-LBD ligand and the AR-LBD ligand is an agonist or antagonist, a partial agonist or partial antagonist, or a SARMs of the AR-LBD.
6. The crystal of claim 5 wherein the agonist is dihydrotestosterone.
7. The crystal of claim 1 having all of the coordinates listed in Table A.
8. The crystal of claim 1 wherein said crystal comprises mammalian AR-LBD protein.
9. The crystal of claim 1 wherein said crystal comprises rat AR-LBD protein.
10. The crystal of claim 1 wherein said AR-LBD ligand has the following unit cell dimensions in angstroms: a = 56.03 ± 5% , b = 66.27 ± 5%, c = 70.38 ± 5% and an orthorhombic space group P212121.
11. A molecule or molecular complex comprising all or any part of the ligand binding site defined by structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877 and F878 according to Table A, or a mutant or homologue of said molecule or molecular complex.

12. The molecule or molecular complex of claim 11 wherein said mutant or homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said AR-LBD amino acids of not more than 1.5 Angstroms or 30% sequence identity with said AR-LBD amino acids.

13. A molecule or molecular complex comprising all or any part of the ligand binding site defined by structure coordinates of AR-LBD amino acids N705, Q711, R752, F764 and T877 according to Table A, or a mutant or homologue of said molecule or molecular complex.

14. The molecule or molecular complex of claim 13 wherein said mutant or homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said AR-LBD amino acids of not more than 1.5 Angstroms or 30% sequence identity with said AR-LBD amino acids.

15. A machine-readable data storage medium comprising a data storage material encoded with machine readable data, wherein the data is defined by the structure coordinates of an AR-LBD/AR-LBD ligand or ligand complex according to Table A or a homologue of said complex, wherein said homologue comprises backbone atoms that have a root mean square deviation from the backbone atoms of the complex of not more than 3.0Å

16. The machine-readable data storage medium according to claim 15, wherein said AR-LBD/AR-LBD ligand or ligand complex is homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 2.0 Å.

17. A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data comprising a Fourier transform of at least a portion of the structural coordinates for an AR-LBD/AR-LBD ligand according to Table A; which, when combined with a second set of machine readable data comprising an X-ray diffraction pattern of a molecule or molecular complex of unknown structure, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, said first set of data and said second set of data.

18. A binding site in AR-LBD for an AR modulator in which a portion of said ligand is in van der Walls contact or hydrogen bonding contact with any portion or all of residues V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD according to Table A.

19. The binding site according to claim 18 wherein the AR-LBD is a homologue or mutant with 25%-95% identity to residues V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD according to Table A.

20. A method of obtaining structural information about a molecule or a molecular complex of unknown structure by using the structure coordinates set forth in Table A, comprising the steps of:

a. generating X-ray diffraction data from said crystallized molecule or molecular complex;

b. applying at least a portion of the structure coordinates set forth in Table A to said X-ray diffraction pattern to generate a three-dimensional electron density map of at least a portion of the molecule or molecular complex; and

c. using all or a portion of the structure coordinates set forth in Table A to generate homology models of AR-LBD or any other nuclear hormone receptor ligand binding domain.

21. A computational method of designing an androgen receptor synthetic ligand comprising:

a. using a three dimensional model of a crystallized protein comprising an AR-LBD/AR-LBD ligand complex to determine

at least one interacting amino acid of the AR-LBD that interacts with at least one first chemical moiety of the AR-LBD ligand; and

b. selecting at least one chemical modification of said first chemical moiety to produce a second chemical moiety with a structure that either decreases or increases an interaction between said interacting amino acid and said second chemical moiety compared to said interaction between said interacting amino acid and said first chemical moiety.

22. A method for identifying a compound that modulates androgen receptor activity, the method comprising any combination of steps of:

a. modeling test compounds that fit spatially into the AR-LBD as defined by structure coordinates according to Table A, or using a three-dimensional structural model of AR-LBD, mutant AR-LBD or AR-LBD homologue or portion thereof;

b. using said structure coordinates or ligand binding site as set forth in claim 18 to identify structural and chemical features;

c. employing identified structural or chemical features to design or select compounds as potential AR modulators;

d. employing the three-dimensional structural model or the ligand binding site to design or select compounds as potential AR modulators;

e. synthesizing the potential AR modulators;

f. screening the potential AR modulators in an assay characterized by binding of a test compound to the AR-LBD; and

g. modifying or replacing one or more amino acids from AR-LBD selected from the group consisting of V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD according to Table A.

23. The method according to claim 22 wherein the potential AR modulator is from a library of compounds.

24. The method according to claim 22 wherein the potential AR modulator is selected from a database.

25. The method according to claim 22 wherein the potential AR modulator is designed *de novo*.

26. The method according to claim 22 wherein the potential AR modulator is designed from a known agonist, partial agonist, antagonist, partial antagonist or SARMs.

27. The method according to claim 22 wherein the potential AR modulator is an agonist or partial agonist and AR activity is measured by translocation or unwinding or helix 12.

28. The method according to claim 22 wherein the potential AR modulator is an antagonist or partial antagonist and AR activity is measured by translocation or unwinding or helix 12.

29. An AR modulator identified by the method of claim 22.

30. A method for treating prostate cancer comprising administering an effective amount of an AR modulator identified by the method of claim 22.

31. A method for treating an age related disease comprising administering an effective amount of an AR modulator identified by the method of claim 22.

32. The method of claim 31 wherein said age related disease is osteoporosis, muscle wasting or loss of libido.

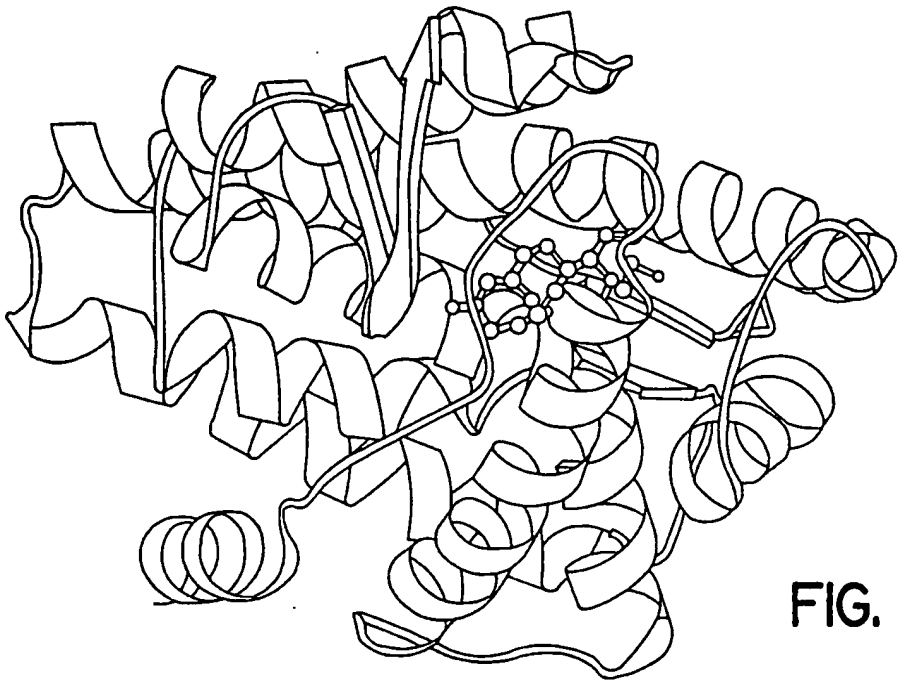


FIG. 1

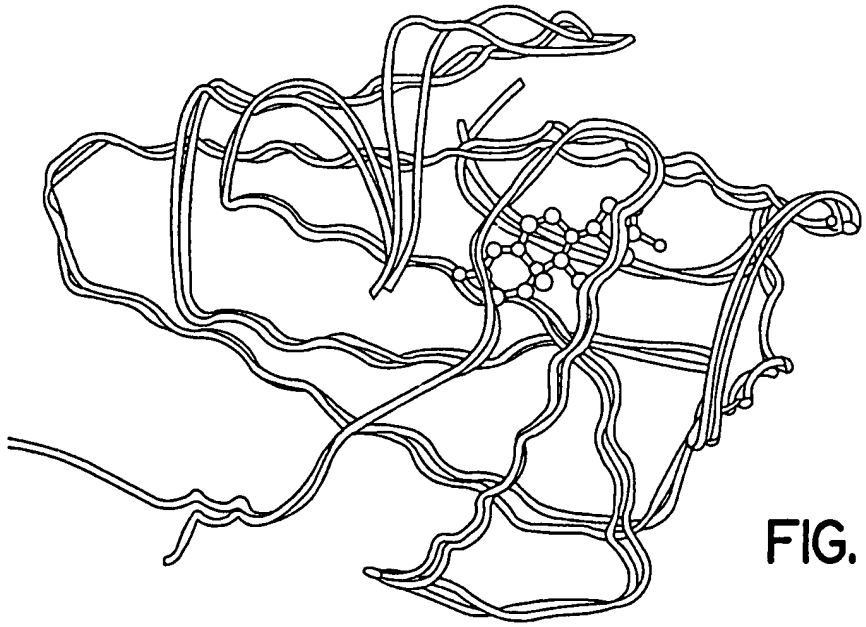


FIG. 2

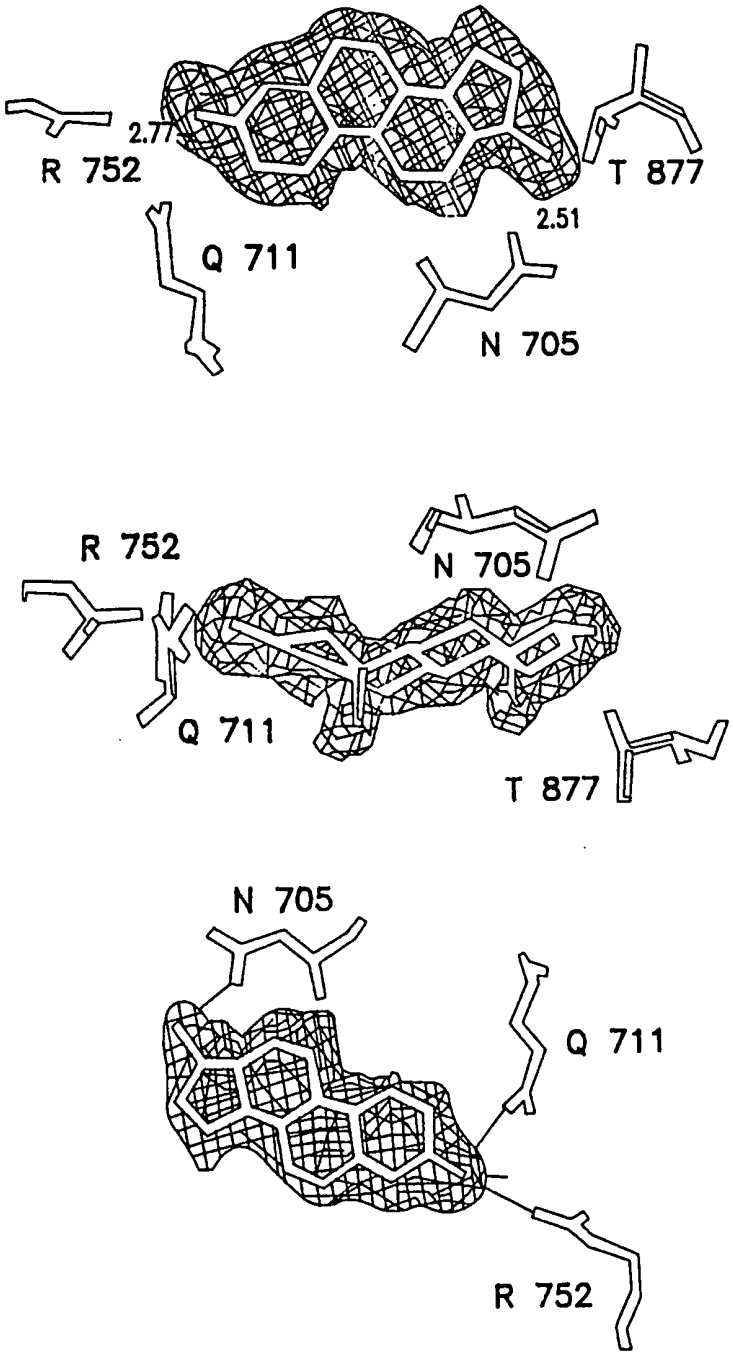
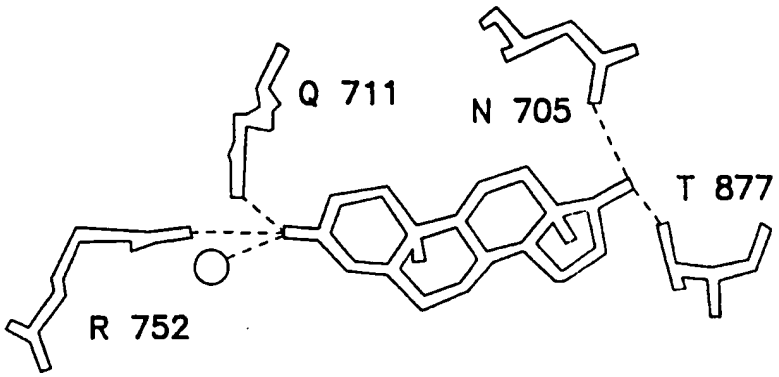

2.77
R 752
T 877
2.51
Q 711
N 705
R 752
N 705
Q 711
T 877
N 705
Q 711
R 752

FIG. 3



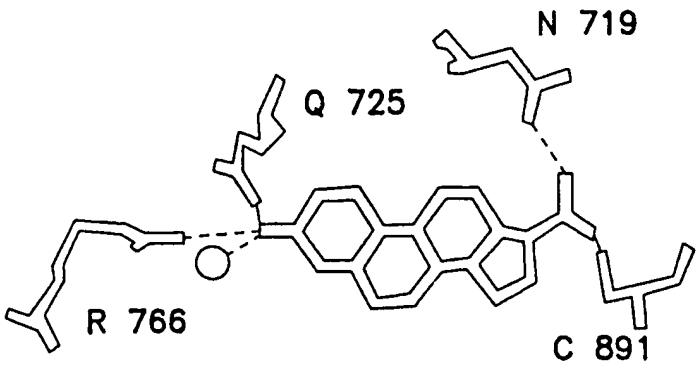


FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/28495

A. CLASSIFICATI N OF SUBJECT MATTER

IPC(7) : G01N 33/53
US CL :435/7.2
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4,7.1,7.2,69.1; 436/501,63; 514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS, EMBASE, MEDLINE, WPI, BIOTECH ABS, covering search terms: crystal, androgen, receptor, inhibitor

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,411,981 A (GAILLARD-KELLY et al.) 02 May 1995, see especially column 9, line 43, through column 10, line 15.	30-32
Y	US 5,434,176 A (CLAUSSNER et al.) 18 July 1995, see especially column 8, line 49, through column 9, line 24.	30-32
A	US 5,298,429 A (EVANS et al.) 29 March 1994, see entire document.	1-32
Y	US 5,693,646 A (JONES et al.) 02 December 1997, see the SUMMARY OF THE INVENTION section in column 2.	11-14, 18, 19, & 29
Y	US 5,854,202 A (DEDHAR) 29 December 1998, see entire document.	11-14, 18, 19, & 29

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

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Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ARDIN MARSCHEL Telephone No. (703) 308-0196

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INTERNATIONAL SEARCH REPORT

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NAKADA et al. The Androgen Receptor Status of Neuroendocrine Cells in Human Benign and Malignant Prostate Tissue. Cancer Research. 01 May 1993, Volume 53, pages 1967-1970, see the entire document.	11-14, 18, 19, & 29
X	EKENA et al. Determinants of Ligand Specificity of Estrogen Receptor-α: Estrogen versus Androgen Discrimination. Journal of Biological Chemistry. 09 January 1998, Volume 273, Number 2, pages 693-699, see especially the abstract.	11-14, 18, 19, & 29
X --- Y	MIYAMOTO et al. Promotion of agonist activity of antiandrogens by the androgen receptor coactivator, ARA70, in human prostate cancer DU154 cells. Proceedings of the National Academy of Sciences, USA. June 1998, Volume 95, pages 7379-7384, see the entire document.	11-14, 18, 19, & 29 ---------- 30
X	SAI et al. An Exonic Point Mutation of the Androgen Receptor Gene in a Family with Complete Androgen Insensitivity. American Journal of Human Genetics. 1990, Volume 46, pages 1095-1100, see especially the abstract and the Introduction on pages 1095-1096.	11-14, 18, 19, & 29